

CANELLA 09/544,644

=> d his

(FILE 'HOME' ENTERED AT 09:11:31 ON 11 APR 2002)

FILE 'REGISTRY' ENTERED AT 09:11:41 ON 11 APR 2002

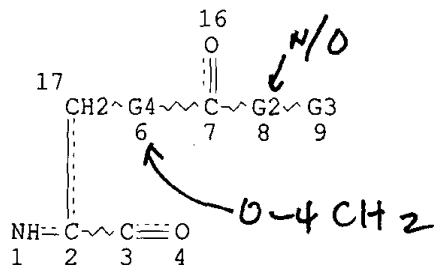
L1 STR
 L2 12 S L1
 L3 1331104 S PROTEIN/FS
 L4 710561 S L3 AND SQL<101 *710,561 peptides w/ 2-100 residues (parent set)*
 L5 4 S L1 SSS SAM SUB=L4
 L6 SCREEN 1992 AND 2005
 L7 SCREEN 2043
 L8 4 S L1 AND L6 NOT L7 SSS SAM SUB=L3
 L9 STR L1
 L10 4 S L9 SSS SAM SUB=L4
 L11 9059 S L9 SSS FUL SUB=L4 *9059 peptides*
 SAVE L11 TEMP CAN664P/A

FILE 'HCAPLUS' ENTERED AT 09:42:36 ON 11 APR 2002

L12 2234 S L11
 L13 28 S L12(L)?CONJUGAT?
 L14 3 S L12(L) (HYDROPHOB? OR LIPOPHIL?)
 L15 0 S L13 AND L14
 L16 71 S L12 AND (HYDROPHOB? OR LIPOPHIL?)
 L17 3 S L13 AND L16
 L18 25 S L13 NOT L17
 L19 1 S L12(L) (DRUG DELIVERY)
 L20 9 S L12(L) (DELIVER? OR TRANSPORT? OR UPTAK? OR ENDOCYTOSIS)
 L21 14 S L14 OR L17 OR L19-20
 L22 1 S 2000:725483/AN
 L23 14 S L21 NOT L22 *14*
 L24 25 S L13 NOT L23 *25 cites*
 L25 82595 S N-TERMIN?
 L26 66233 S C-TERMIN?
 L27 1876 S CONJUGAT?(L) L25-26
 L28 910 S L27(L) PEPTID?
 L29 55 S L28(L) (HYDROPHOB? OR LIPOPHIL?)
 L30 12 S L29(L) (DELIVER? OR TRANSPORT? OR UPTAK? OR ENDOCYTOSIS)

=> d que 112

L3 1331104 SEA FILE=REGISTRY ABB=ON PLU=ON PROTEIN/FS
 L4 710561 SEA FILE=REGISTRY ABB=ON PLU=ON L3 AND SQL<101
 L9 STR₁



Ak @10

O~Ak
@11 12

Cb @15

Cb @13



↑
cyclohydrocarbon

VAR G2=O/NH
 VAR G3=10/11/13/15
 REP G4=(0-4) CH2
 NODE ATTRIBUTES:
 CONNECT IS E3 RC AT 2
 CONNECT IS E1 RC AT 10
 CONNECT IS E1 RC AT 12
 DEFAULT MLEVEL IS ATOM
 GGCAT IS MCY SAT AT 13
 GGCAT IS MCY UNS AT 15
 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS M2 C AT 10
 ECOUNT IS M2 C AT 12
 ECOUNT IS X6 C AT 13
 ECOUNT IS E6 C AT 15

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L11 9059 SEA FILE=REGISTRY SUB=L4 SSS FUL L9
 L12 2234 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

=> d ibib abs hitstr 1

L23 ANSWER 1 OF 14 HCAPLUS, COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:240709 HCAPLUS

DOCUMENT NUMBER: 135:55450

TITLE: Peptide transport by the multidrug resistance protein MRP1

AUTHOR(S): De Jong, Mariska C.; Slootstra, Jerry W.; Scheffer, George L.; Schroeijsers, Anouk B.; Puijk, Wouter C.; Dinkelberg, Remco; Kool, Marcel; Broxterman, Henk J.; Meloen, Rob H.; Scheper, Rik J.

CORPORATE SOURCE: Department of Pathology, University Hospital Vrije Universiteit, Amsterdam, 1081 HV, Neth.

SOURCE: Cancer Research (2001), 61(6), 2552-2557

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Small hydrophobic peptides were studied as possible substrates of the multidrug resistance protein (MRP)-1 (ABCC1) transmembrane transporter mol. As obsd. earlier for P-glycoprotein- (Pgp; ABCB1) overexpressing cells, MRP1-overexpressing cells, including cells stably transfected with the MRP1 cDNA, showed distinct resistance to the cytotoxic peptide N-acetyl-Leu-Leu-norleucinal (ALLN). Resistance to this peptide and another toxic peptide deriv., which is based on a Thr-His-Thr-Nle-Glu-Gly backbone conjugated to Bu and benzyl groups (4A6), could be reversed by MRP1 inhibitors. The reduced toxicity of 4A6 in MRP1-overexpressing cells was assocd. with lower accumulation of a fluorescein-labeled deriv. of this peptide. Glutathione (GSH) depletion had a clear effect on resistance to ALLN but hardly affected 4A6 resistance. In a limited structure-activity study using peptides that are analogous to 4A6, MRP1-overexpressing cells were resistant to these peptides as well. Remarkably, when selecting A2780 ovarian cancer cells for resistance to ALLN, even in the absence of Pgp blockers, resulting cell lines had up-regulated MRP1, rather than any of the other currently known multidrug resistance transporter mols. including Pgp, MRP2 (ABCC2), MRP3 (ABCC3), MRP5 (ABCC5), and the breast cancer resistance protein ABCG2. ALLN-resistant, MRP1-overexpressing cells were cross-resistant to 4A6 and the classical multidrug resistance drugs doxorubicin, vincristine, and etoposide. This establishes MRP1 as a transporter for small hydrophobic peptides. More extensive structure-activity relation studies should allow the identification of clin. useful peptide antagonists of MRP1.

IT 345662-87-5 345662-88-6 345662-89-7

345662-90-0 345662-91-1 345662-93-3

345662-94-4 345662-95-5 345662-96-6

345662-97-7 345662-99-9 345663-00-5

345663-01-6 345663-02-7 345663-36-7

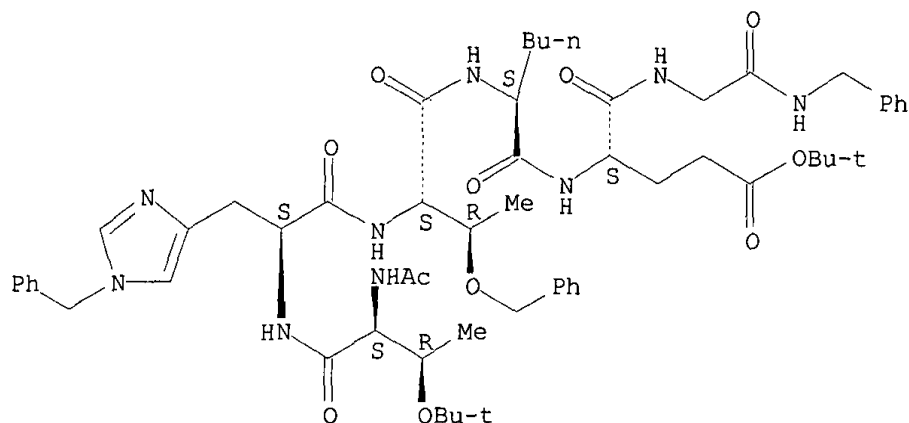
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(peptide **transport** by multidrug resistance protein MRP1)

RN 345662-87-5 HCAPLUS

CN Glycinamide, N-acetyl-O-(1,1-dimethylethyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

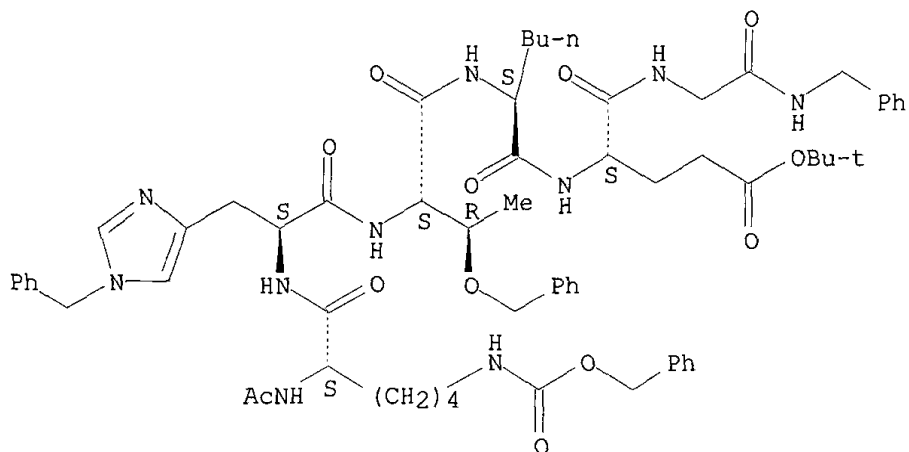
Absolute stereochemistry.



RN 345662-88-6 HCAPLUS

CN Glycinamide, N2-acetyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

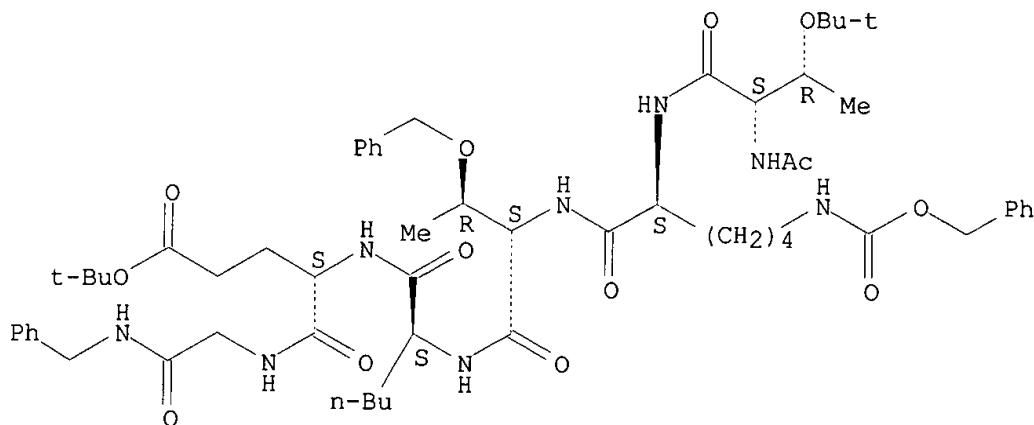
Absolute stereochemistry.



RN 345662-89-7 HCAPLUS

CN Glycinamide, N-acetyl-O-(1,1-dimethylethyl)-L-threonyl-N6-
[(phenylmethoxy)carbonyl]-L-lysyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-
L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA
INDEX NAME)

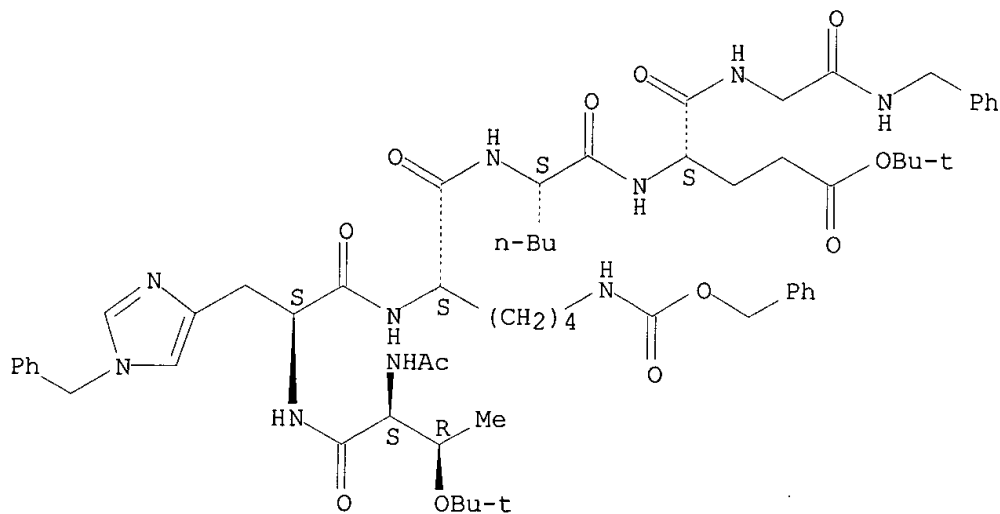
Absolute stereochemistry.



RN 345662-90-0 HCAPLUS

CN Glycinamide, N-acetyl-O-(1,1-dimethylethyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

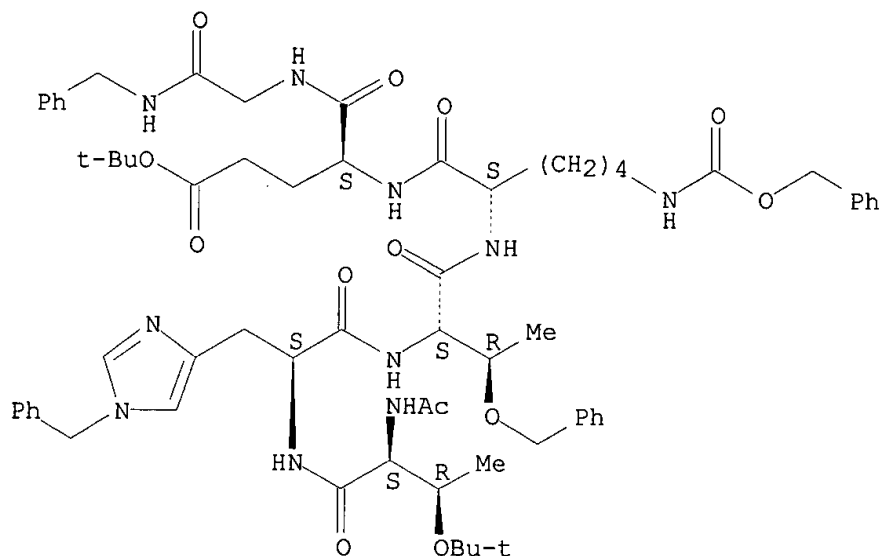
Absolute stereochemistry.



RN 345662-91-1 HCAPLUS

CN Glycinamide, N-acetyl-O-(1,1-dimethylethyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

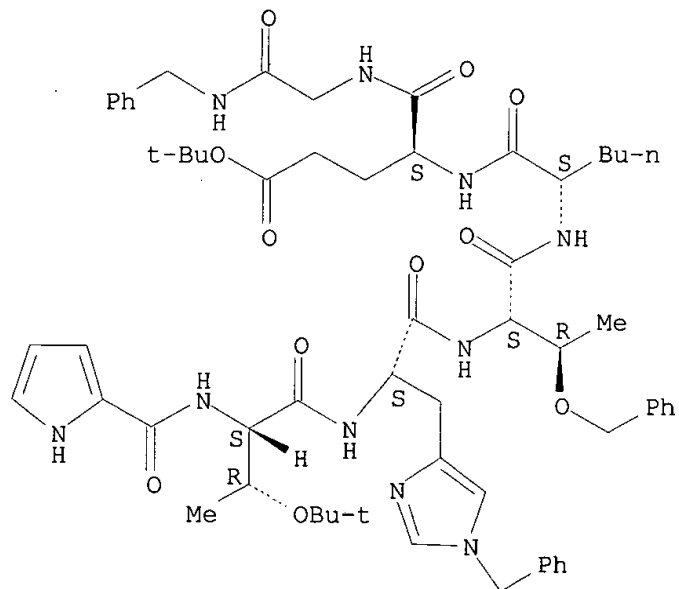
Absolute stereochemistry.



RN 345662-93-3 HCAPLUS

CN Glycinamide, 2,3,4,5-tetradehydropropyl-O-(1,1-dimethylethyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

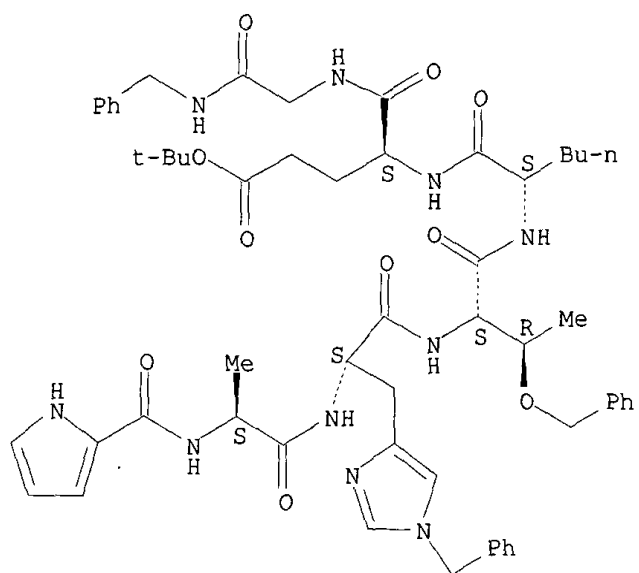
Absolute stereochemistry.



RN 345662-94-4 HCAPLUS

CN Glycinamide, 2,3,4,5-tetradehydropropyl-L-alanyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

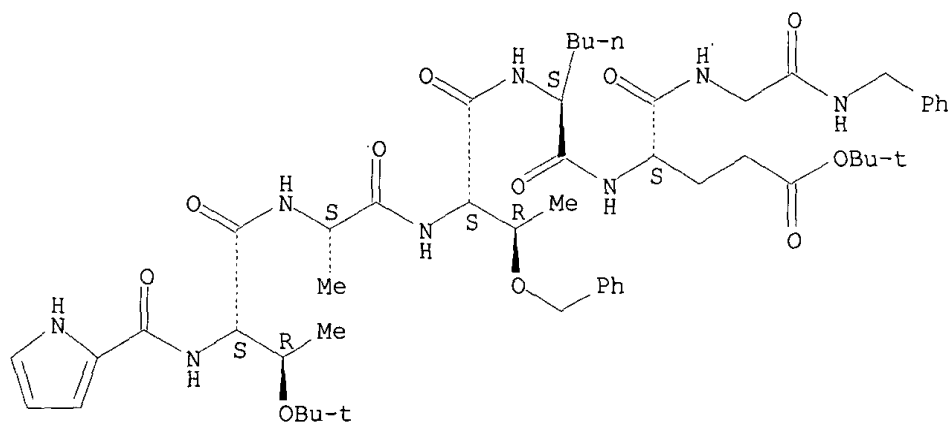
Absolute stereochemistry.



RN 345662-95-5 HCAPLUS

CN Glycinamide, 2,3,4,5-tetradehydropropyl-O-(1,1-dimethylethyl)-L-threonyl-L-alanyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

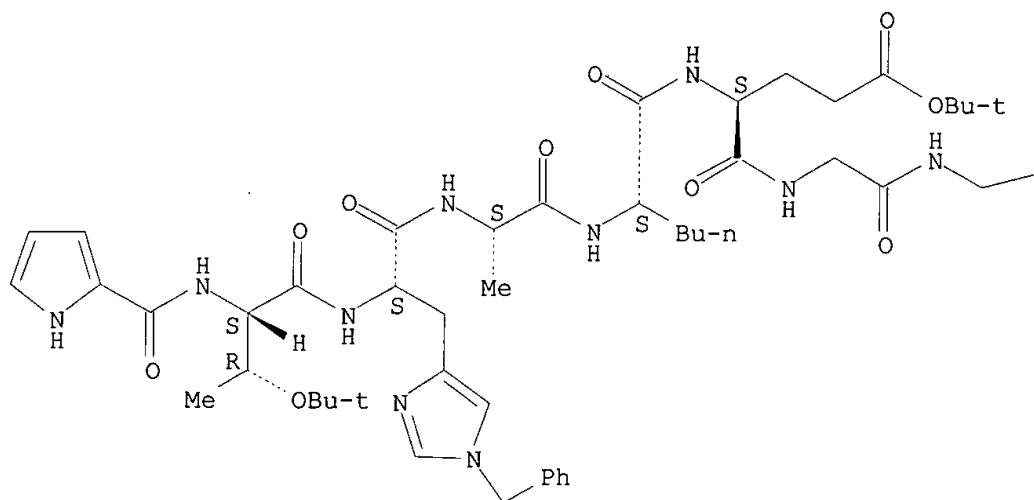


RN 345662-96-6 HCAPLUS

CN Glycinamide, 2,3,4,5-tetradehydropropyl-O-(1,1-dimethylethyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-L-alanyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



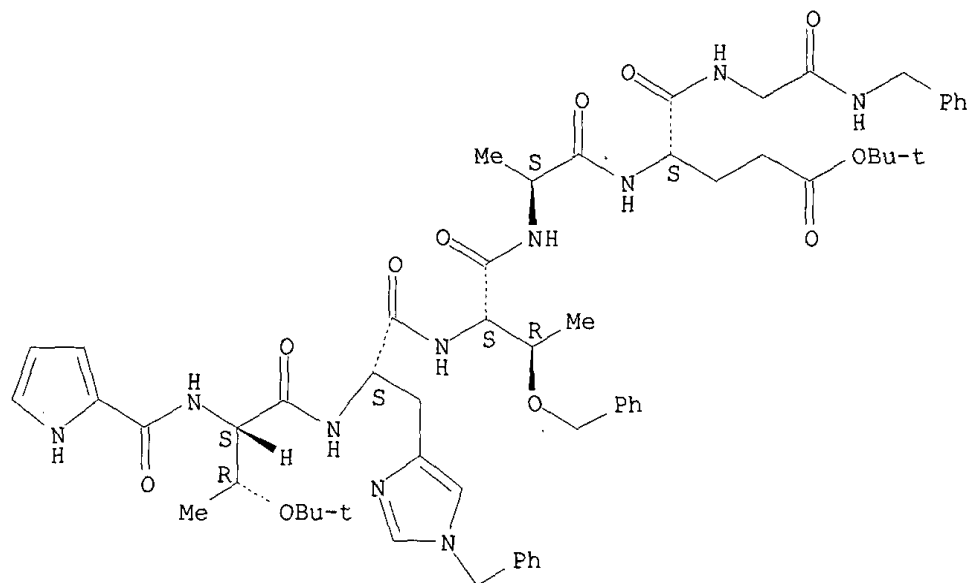
PAGE 1-B

— Ph

RN 345662-97-7 HCAPLUS

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Absolute stereochemistry.

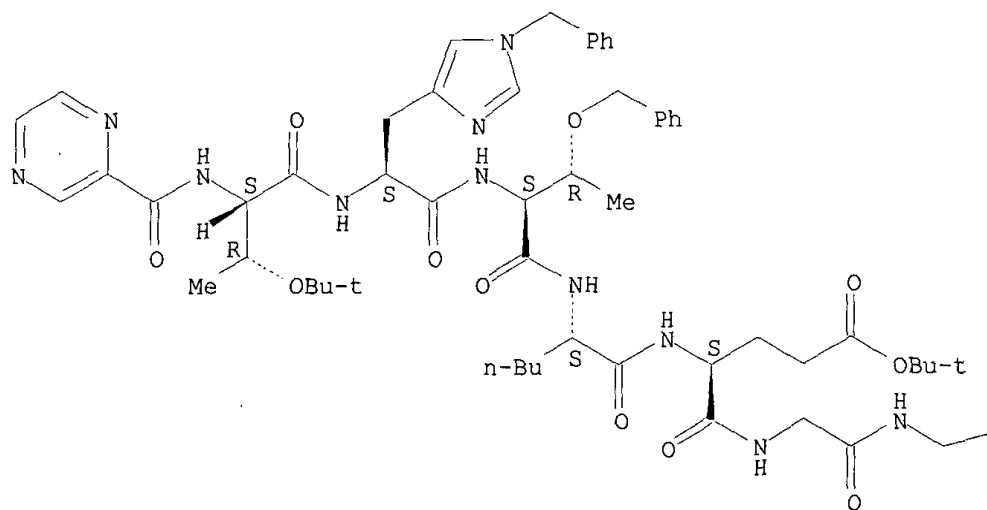


RN 345662-99-9 HCAPLUS

CN Glycinamide, O-(1,1-dimethylethyl)-N-(pyrazinylcarbonyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

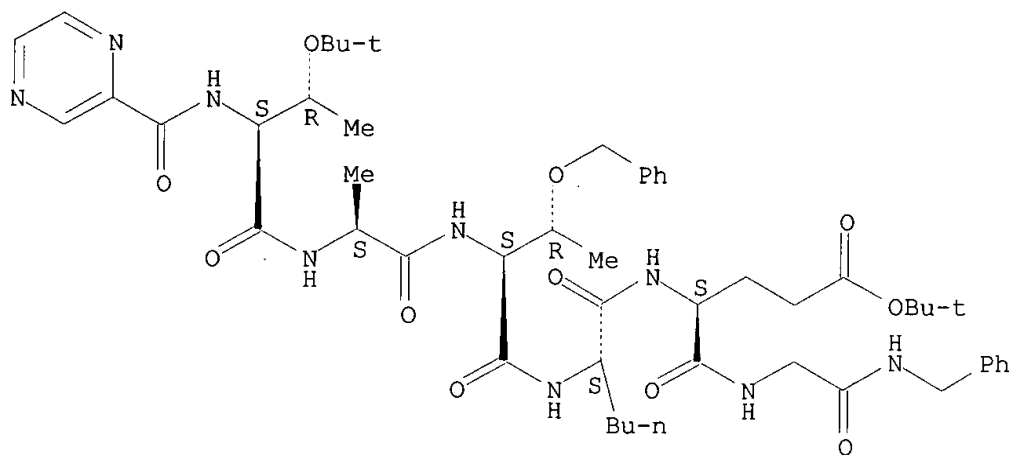


— Ph

RN 345663-00-5 HCAPLUS

CN Glycinamide, O-(1,1-dimethylethyl)-N-(pyrazinylcarbonyl)-L-threonyl-L-alanyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

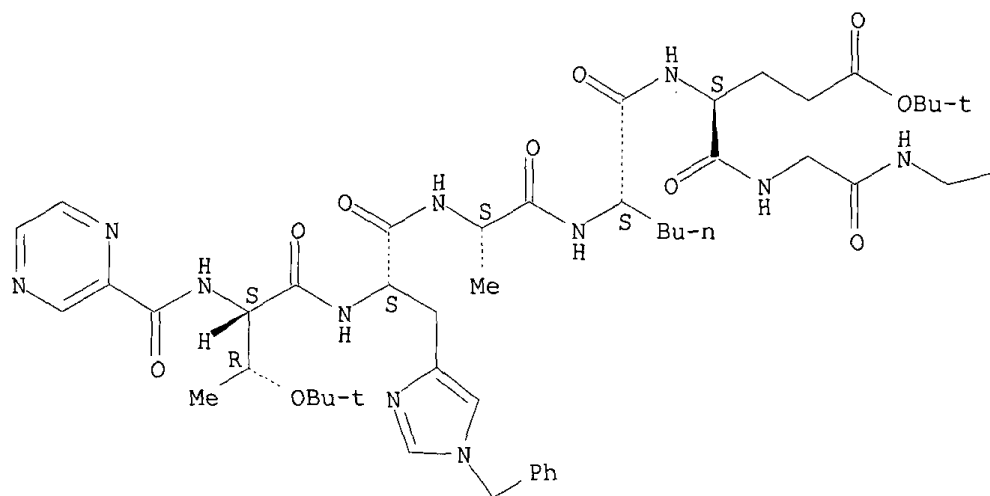


RN 345663-01-6 HCAPLUS

CN Glycinamide, O-(1,1-dimethylethyl)-N-(pyrazinylcarbonyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-L-alanyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

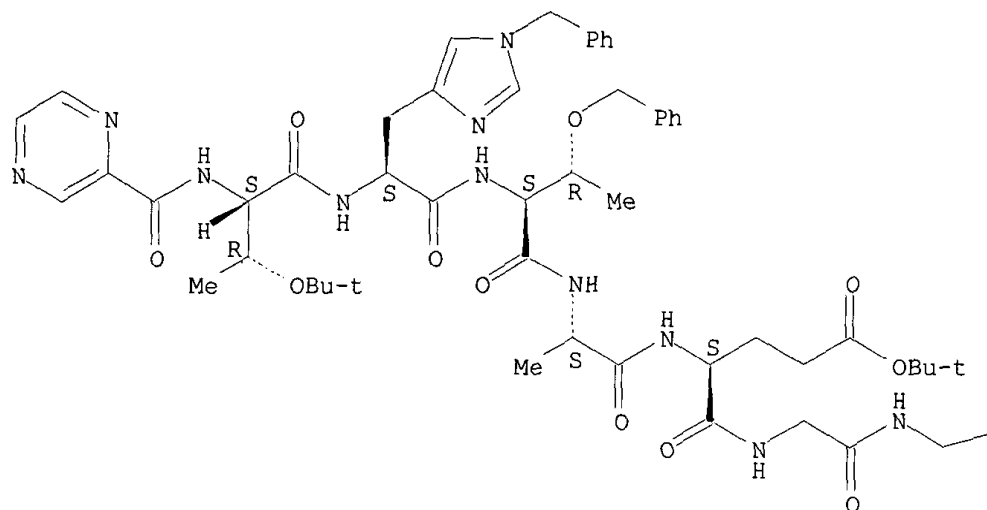
Ph

RN 345663-02-7 HCAPLUS

CN Glycinamide, O-(1,1-dimethylethyl)-N-(pyrazinylcarbonyl)-L-threonyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-alanyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



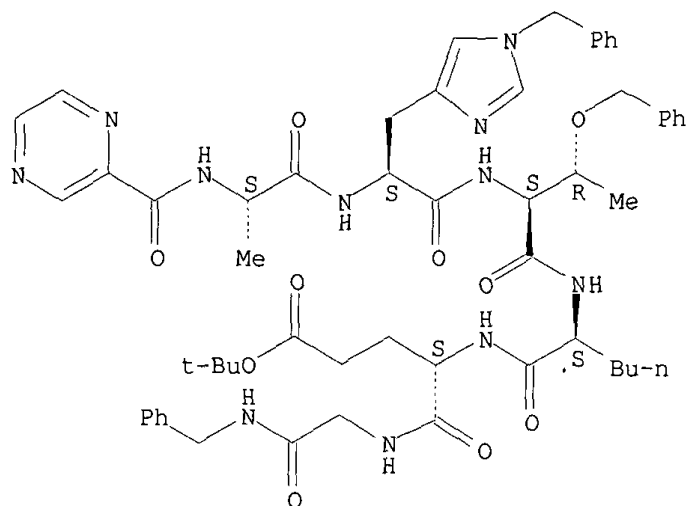
PAGE 1-B

— Ph

RN 345663-36-7 HCAPLUS

CN Glycinamide, N-(pyrazinylcarbonyl)-L-alanyl-1-(phenylmethyl)-L-histidyl-O-(phenylmethyl)-L-threonyl-L-norleucyl-L-.alpha.-glutamyl-N-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

36

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L23 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:441598 HCAPLUS
 DOCUMENT NUMBER: 133:79334
 TITLE: Therapeutic delivery using compounds self-assembled
 into high axial ratio microstructures
 INVENTOR(S): Yager, Paul; Gelb, Michael H.; Lukyanov, Anatoly N.;
 Goldstein, Alex S.; Disis, Mary L.
 PATENT ASSIGNEE(S): University of Washington, USA
 SOURCE: PCT Int. Appl., 89 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 2000037046 | A1 | 20000629 | WO 1999-US30931 | 19991221 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6180114 | B1 | 20010130 | US 1998-219057 | 19981222 |
| EP 1146855 | A1 | 20011024 | EP 1999-966656 | 19991221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-219057 | A 19981222 |
| | | | US 1996-752848 | A2 19961121 |
| | | | US 1998-87179P | P 19980529 |
| | | | WO 1999-US30931 | W 19991221 |

OTHER SOURCE(S): MARPAT 133:79334

AB Therapeutic complexes comprising plural therapeutic compds. self assembled into high axial ratio microstructures are described. The therapeutic complexes satisfy the formula HARM-Th, wherein HARM is a high axial ratio forming material and Th is a therapeutic coupled to or assocd. with the HARM. The therapeutic complexes also can satisfy the formula HARM-S-Th, wherein S is a spacer. Release of the therapeutic by the complex generally follows either 0-order kinetics or pseudo-first order kinetics. A method for delivering therapeutics to organisms, particularly humans, also is described. The method comprises administering an effective amt. of (1) a ligand, such as a therapeutic, self-assembled into a HAR microstructure, or (2) a ligand, such as a therapeutic, coupled to or assocd. with a material capable of thereafter self-assembling into a high axial ratio microstructure, to the mammal. Nucleic acids are an example of a ligand that can be administered effectively according to this method through noncovalent attachment to the HARM-forming materials.

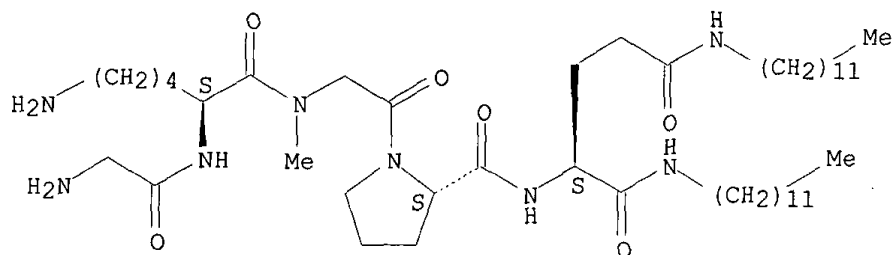
IT 191354-73-1

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (therapeutic **delivery** using compds. self-assembled into high axial ratio microstructures)

RN 191354-73-1 HCAPLUS

CN L-Glutamamide, glycyl-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



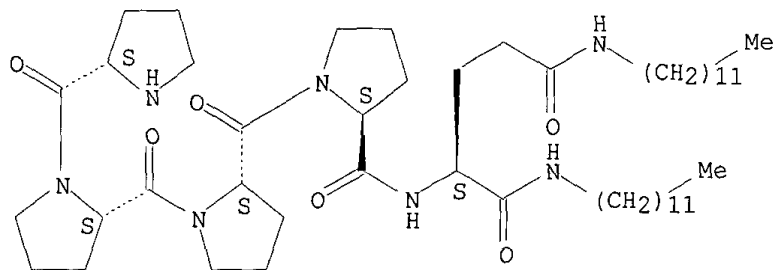
IT 129368-18-9 191354-81-1 191354-89-9
278602-89-4 278602-91-8

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(therapeutic **delivery** using compds. self-assembled into high axial ratio microstructures)

RN 129368-18-9 HCAPLUS

CN L-Glutamamide, L-prolyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-didodecyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

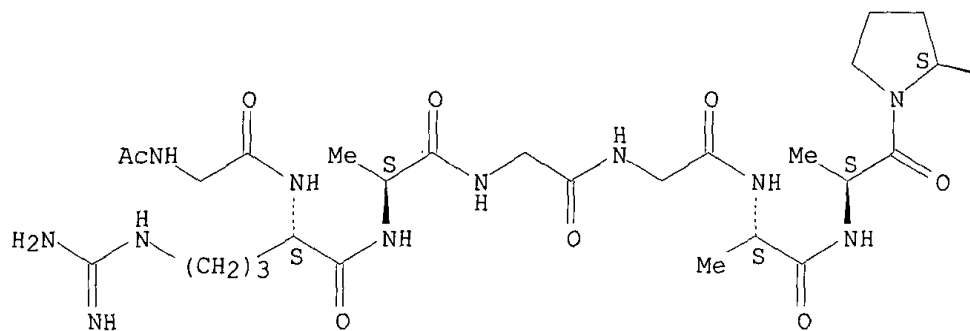


RN 191354-81-1 HCAPLUS

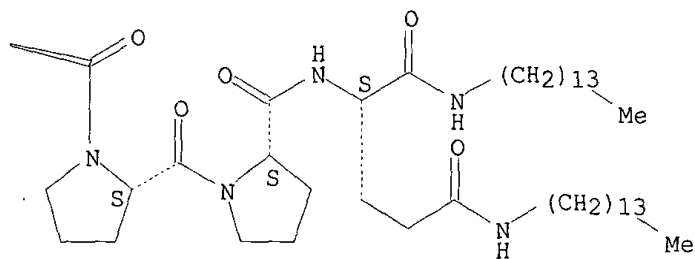
CN L-Glutamamide, N-acetylglycyl-L-arginyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



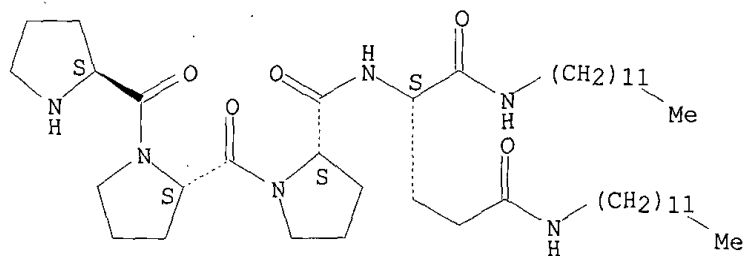
PAGE 1-B



RN 191354-89-9 HCAPLUS

CN L-Glutamamide, L-prolyl-L-prolyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

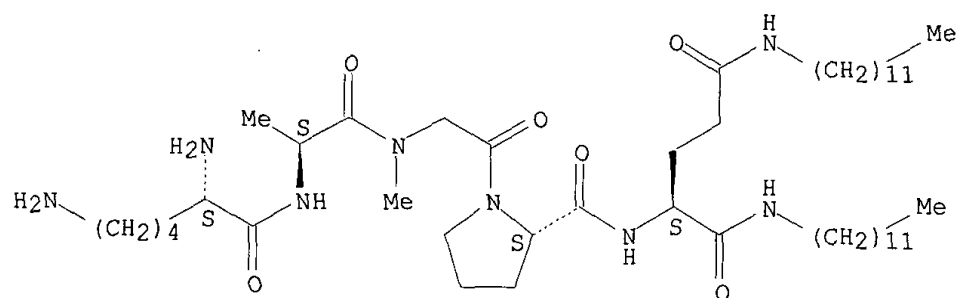
Absolute stereochemistry.



RN 278602-89-4 HCAPLUS

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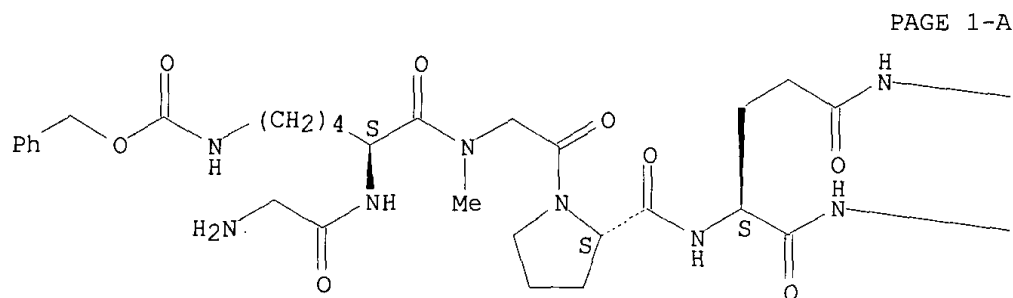
Absolute stereochemistry.



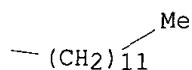
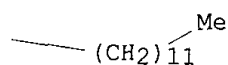
RN 278602-91-8 HCAPLUS

CN L-Glutamamide, glycyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



IT 191354-80-0P 191354-83-3P 191354-87-7P

278602-92-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

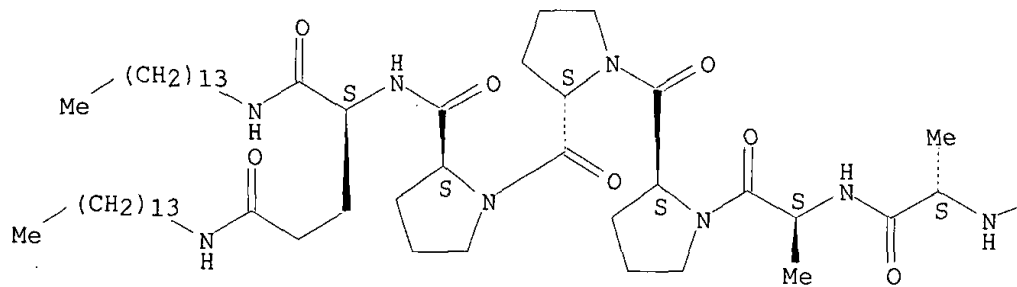
(therapeutic **delivery** using compds. self-assembled into high axial ratio microstructures)

RN 191354-80-0 HCAPLUS

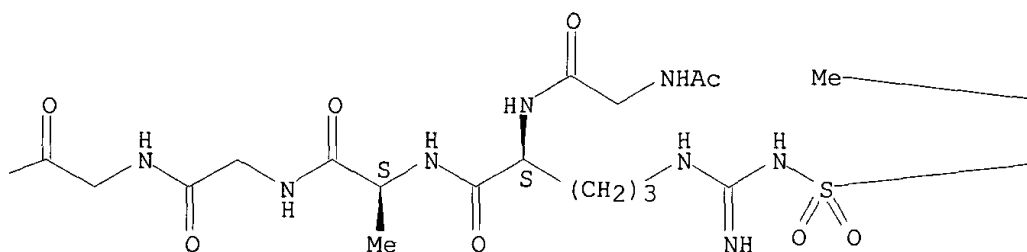
CN L-Glutamamide, N-acetylglycyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

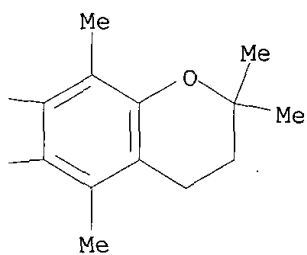
PAGE 1-A



PAGE 1-B



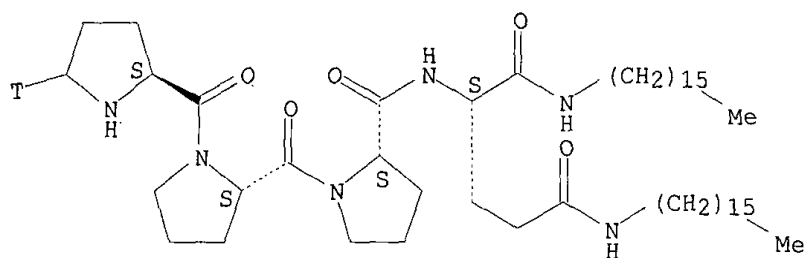
PAGE 1-C



RN 191354-83-3 HCAPLUS

CN L-Glutamamide, L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl-,
monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

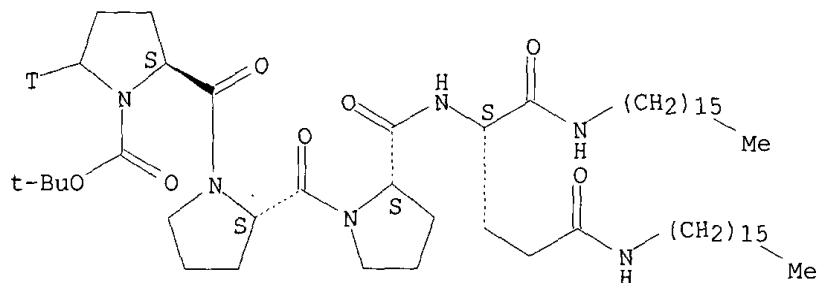


● HCl

RN 191354-87-7 HCAPLUS

CN L-Glutamamide, 1-[(1,1-dimethylethoxy)carbonyl]-L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 278602-92-9 HCAPLUS

CN L-Glutamamide, glycyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-alanyl-glycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

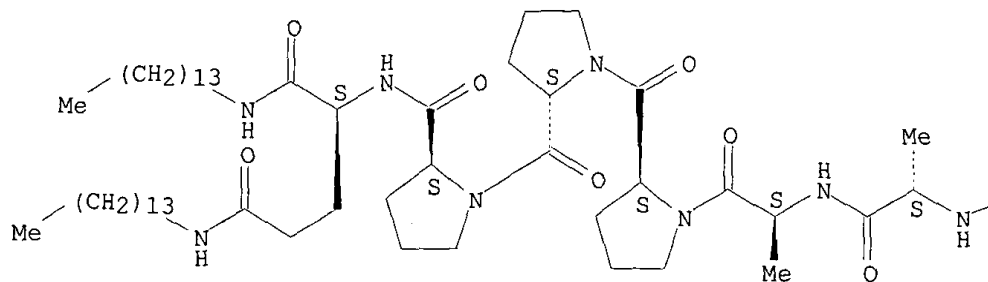
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CRN 239447-17-7

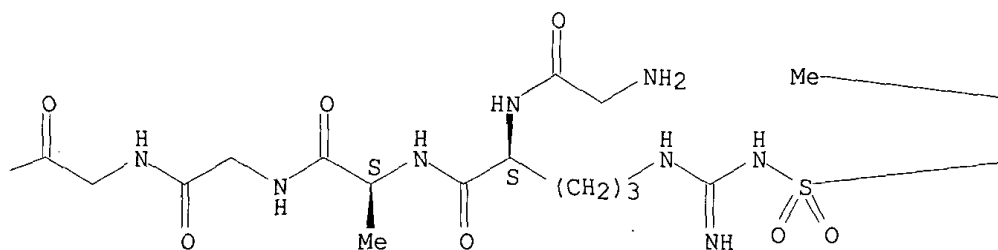
CMF C83 H142 N16 O15 S

Absolute stereochemistry.

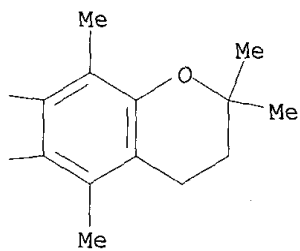
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PAGE 1-B



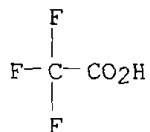
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



REFERENCE COUNT:

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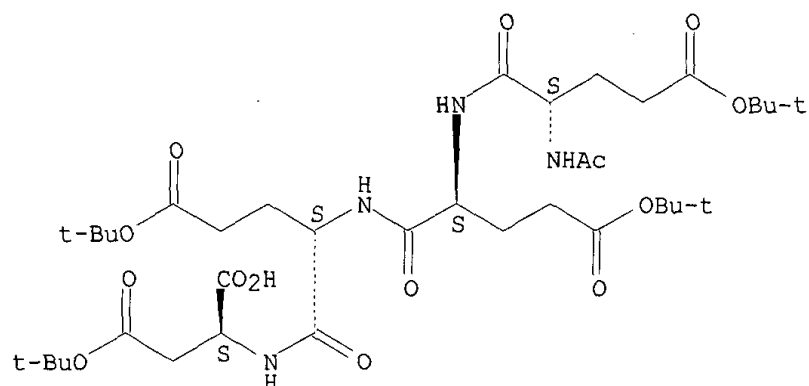
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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L23 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:383983 HCAPLUS
 DOCUMENT NUMBER: 133:34431
 TITLE: Transport system conjugate
 INVENTOR(S): Imfeld, Dominik; Ludin, Christian; Schreier, Thomas
 PATENT ASSIGNEE(S): Pentapharm A.-G., Switz.
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|---|----------|-----------------|------------|
| WO 2000032235 | A1 | 20000608 | WO 1999-CH567 | 19991126 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1133317 | A1 | 20010919 | EP 1999-955629 | 19991126 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 2002035243 | A1 | 20020321 | US 2001-866824 | 20010529 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | CH 1998-2354 | A 19981126 |
| | | | WO 1999-CH567 | W 19991126 |
| OTHER SOURCE(S): MARPAT 133:34431 | | | | |
| AB | A pharmaceutical and/or cosmetic active agent is conjugated, directly or via a linker, to an amino or carboxyl group on substituent Y of a lipophilic compd. Y(NHCnH2n)rC(O)R [Y = amino acid or di- or tripeptide having .gtoreq.3 reactive NH2 and/or CO2H groups, or a C2-8 triamine; RC(O) = (substituted) C4-24 fatty acyl; n = 2, 3; r = 0, 1], where another amino group on Y is attached to a group C(O)(CH2)mCH(SH)CH2(CHR1)pSH or its cyclic disulfide deriv., to facilitate transmembrane transport of the active agent into fibroblasts, keratinocytes, melanocytes, and Langerhans cells of the skin. Thus, .alpha.-MSH-induced melanin formation in S91 melanocytes was inhibited by treating the cells with a conjugate of tyrosinase-mimicking peptide with the transporter H-Lys(.epsilon.-DL-6,8-dithiooctanamide)- NHCH2CH2NHC(O)(CH2)6CH3. Similarly, conjugates of cell growth modulators can be used to inhibit hyperproliferation of keratinocytes in treatment of psoriasis. | | | |
| IT | 273928-68-0P 273928-73-7P 273928-76-0P 273928-77-1P 273928-78-2P 273928-83-9P 273928-87-3P 273928-89-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (transport system conjugate) | | | |
| RN | 273928-68-0 HCAPLUS | | | |
| CN | L-Aspartic acid, N-acetyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.- glutamyl-, 1,2,3,44-tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME) | | | |

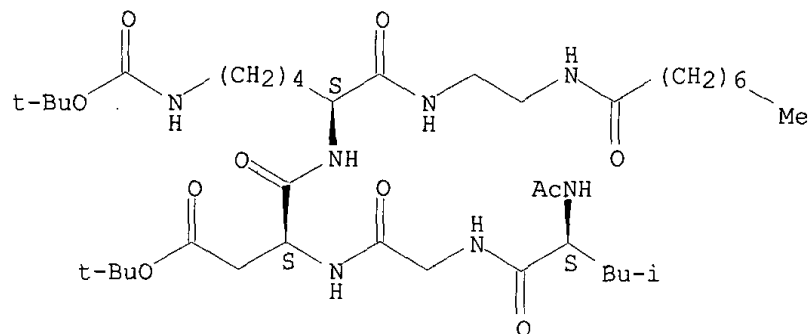
Absolute stereochemistry.



RN 273928-73-7 HCAPLUS

CN L-Lysinamide, N-acetyl-L-leucylglycyl-L-.alpha.-aspartyl-N6-[(1,1-dimethylethoxy)carbonyl]-N-[2-[(1-oxooctyl)amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

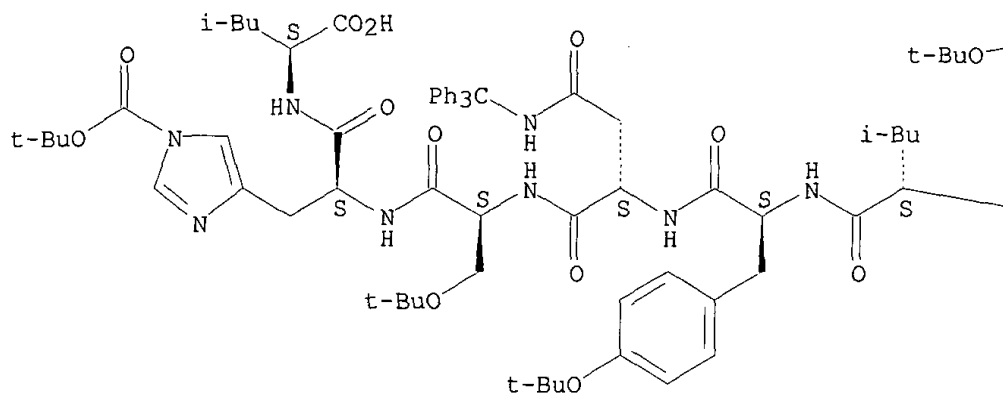


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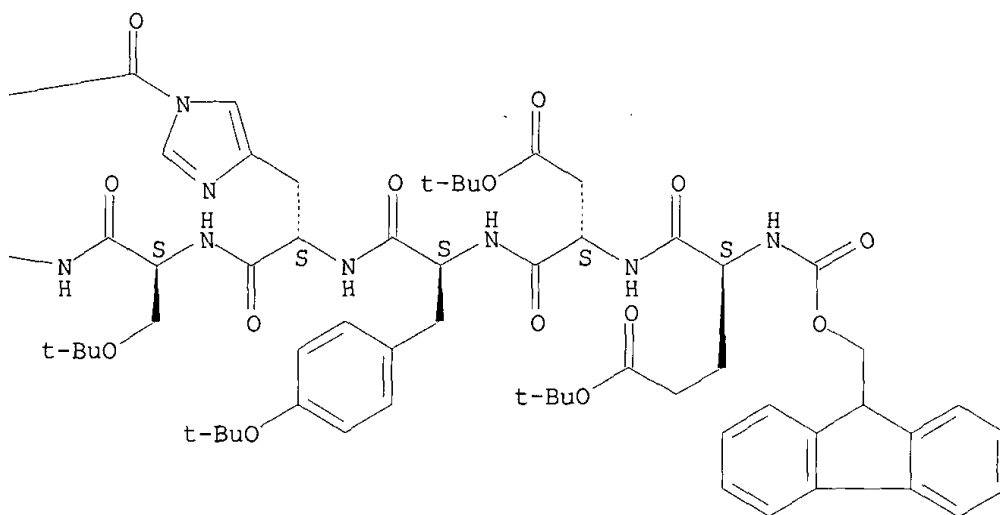
CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-O-(1,1-dimethylethyl)-L-seryl-L-leucyl-O-(1,1-dimethylethyl)-L-tyrosyl-N-(triphenylmethyl)-L-asparaginyl-O-(1,1-dimethylethyl)-L-seryl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-, 1,2-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B

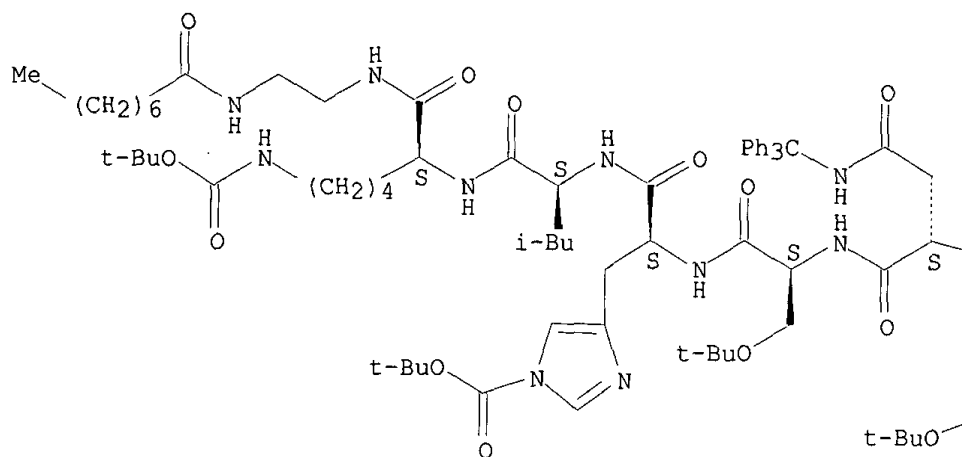


RN 273928-77-1 HCAPLUS

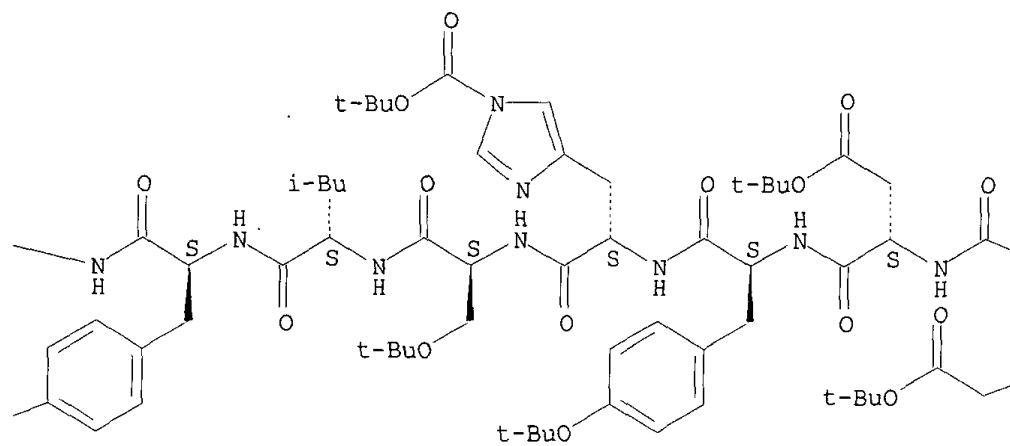
CN L-Lysinamide, N-[(9H-fluorenyl-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-O-(1,1-dimethylethyl)-L-seryl-L-leucyl-O-(1,1-dimethylethyl)-L-tyrosyl-N-(triphenylmethyl)-L-asparaginyl-O-(1,1-dimethylethyl)-L-seryl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-L-leucyl-N6-[(1,1-dimethylethoxy)carbonyl]-N-[2-[(1-oxooctyl)amino]ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

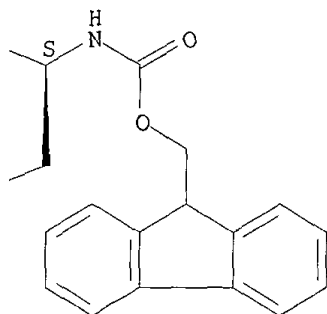
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



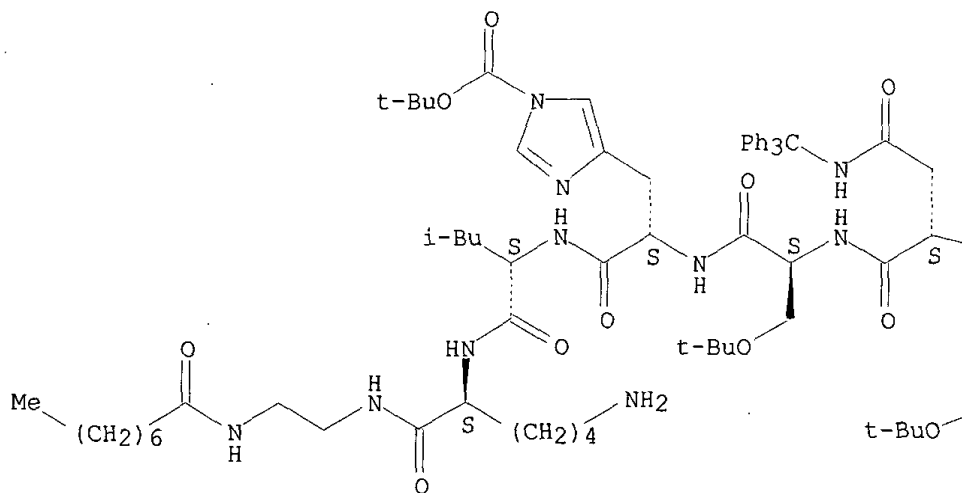


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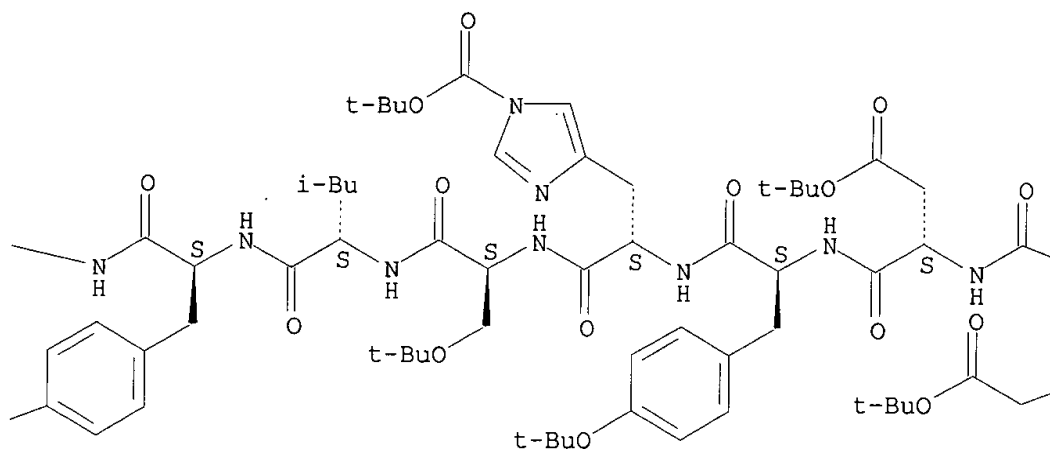
CN L-Lysinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-O-(1,1-dimethylethyl)-L-seryl-L-leucyl-O-(1,1-dimethylethyl)-L-tyrosyl-N-(triphenylmethyl)-L-asparaginyl-O-(1,1-dimethylethyl)-L-seryl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-L-leucyl-N-[2-[(1-oxooctyl)amino]ethyl]-, bis(1,1-dimethylethyl) ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

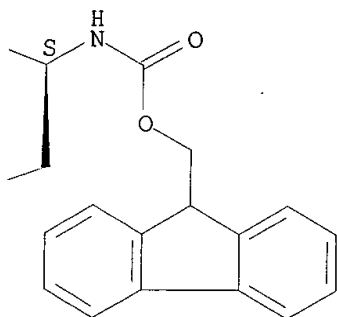
PAGE 1-A



PAGE 1-B



PAGE 1-C

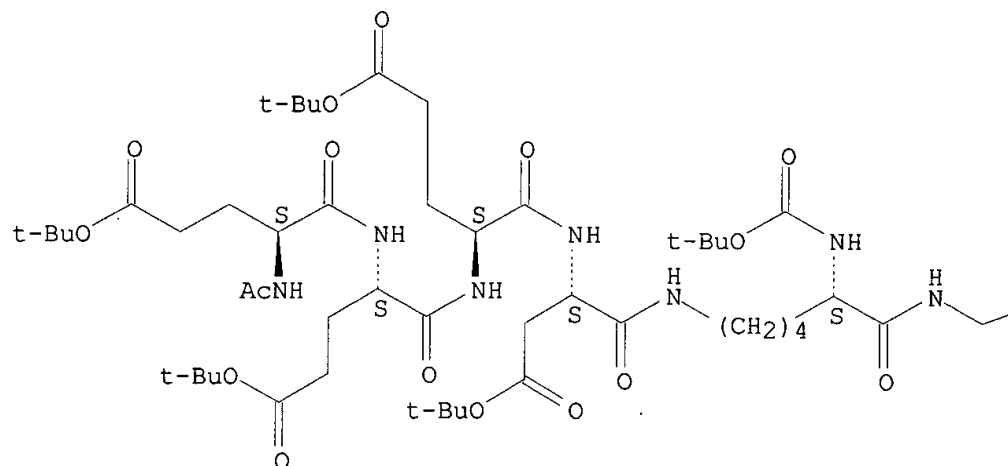


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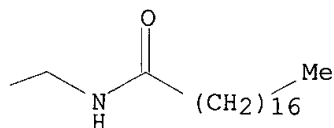
CN L-Lysinamide, N6-(N-acetyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl)-N2-[(1,1-dimethylethoxy)carbonyl]-N-[2-[(1-oxooctadecyl)amino]ethyl]-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

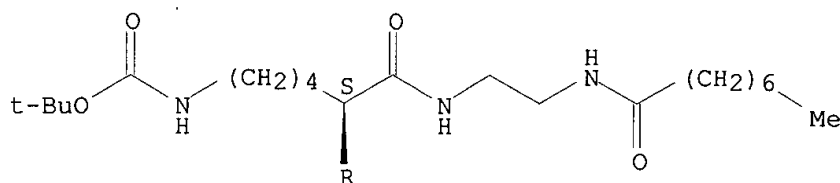


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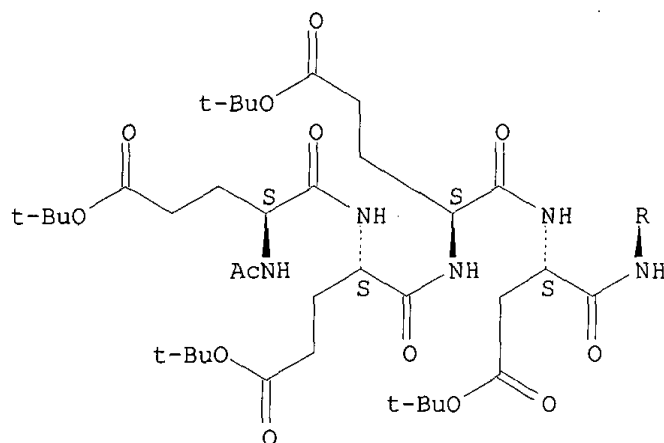
CN L-Lysinamide, N-acetyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-N6-[(1,1-dimethylethoxy)carbonyl]-N-[2-[(1-oxooctyl)amino]ethyl]-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

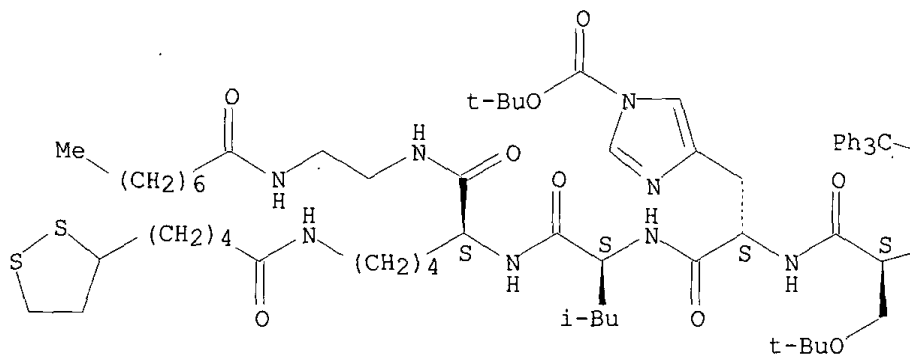


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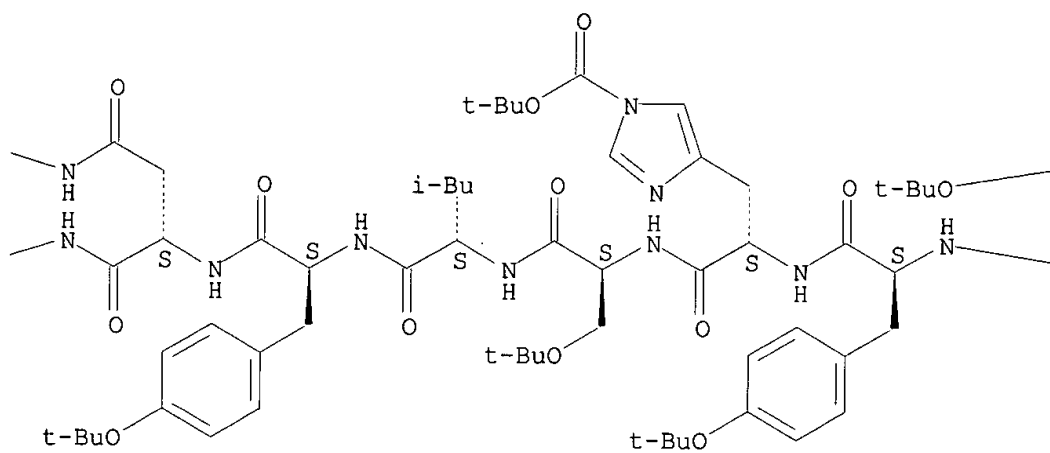
CN L-Lysinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-O-(1,1-dimethylethyl)-L-seryl-L-leucyl-O-(1,1-dimethylethyl)-L-tyrosyl-N-(triphenylmethyl)-L-asparaginyl-O-(1,1-dimethylethyl)-L-seryl-1-[(1,1-dimethylethoxy)carbonyl]-L-histidyl-L-leucyl-N6-[5-(1,2-dithiolan-3-yl)-1-oxopentyl]-N-[2-[(1-oxooctyl)amino]ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

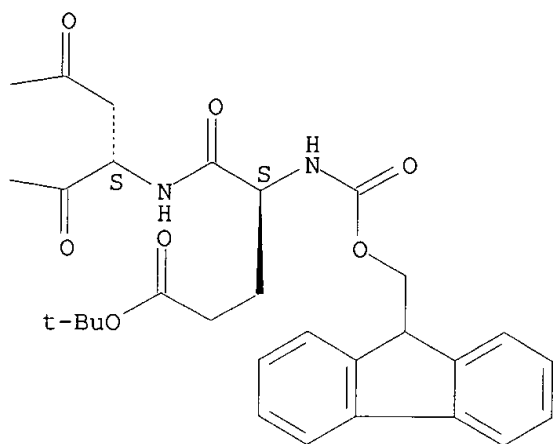
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PAGE 1-B



PAGE 1-C



REFERENCE COUNT:

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THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L23 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:94050 HCAPLUS

DOCUMENT NUMBER: 132:308627

TITLE: The conformation of denovo designed amphiphilic peptides with six or nine L-2-(2,2,2-trifluoroethyl)glycines as the hydrophobic amino acid

AUTHOR(S): Arai, Toru; Imachi, Takashi; Kato, Tamaki; Nishino, Norikazu

CORPORATE SOURCE: Dep. Appl. Chem., Fac. Eng., Kyushu Institute of Technology, Tobata-ku, Kitakyushu, 804-8550, Japan

SOURCE: Bull. Chem. Soc. Jpn. (2000), 73(2), 439-445

CODEN: BCSJAB; ISSN: 0009-2673

PUBLISHER: Chemical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amphiphilic 21-peptides contg. six and nine L-2-(2,2,2-trifluoroethyl)glycines (L-Tfeg) as the hydrophobic amino acids and lysine and glutamic acid as the hydrophilic amino acids were synthesized. The CD spectra showed that these peptides with L-Tfeg took a random conformation in H₂O. On the contrary, similar amphiphilic 21-peptides with leucine as the hydrophobic amino acids took a helical conformation in H₂O. The peptides with L-Tfeg took a helical conformation in H₂O contg. a greater than 20% vol. of 2,2,2-trifluoroethanol. These facts suggested the hydrophobic nature of L-Tfeg. The peptide with six L-Tfeg residues took a helical structure in methanol, however it slowly changed into the .beta.-structure within 24 h. Interestingly, the peptide with nine L-Tfeg residues formed a stable helix under the same conditions. The peptide with nine L-Tfeg residues preferred a helical structure, probably because assembling of the Tfeg side chains was more effective in forming its helix rather than the .beta.-structure.

IT 266325-39-7P 266325-40-0P 266325-41-1P

266325-42-2P 266325-59-1P 266325-60-4P

266325-62-6P 266325-63-7P 266325-65-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and conformation of amphiphilic peptides contg.

(2,2,2-trifluoroethyl)glycines as **hydrophobic** amino acids

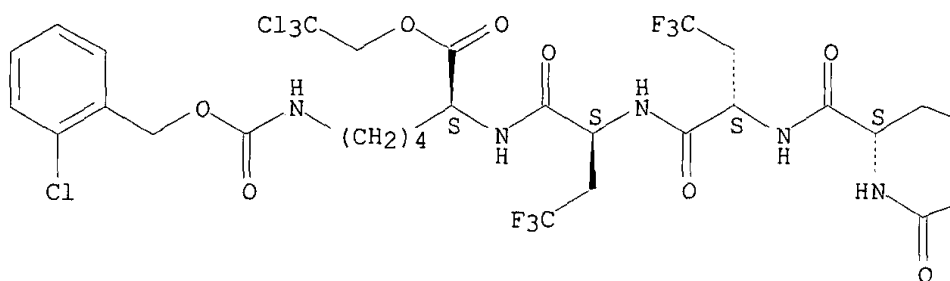
along with Lys and Glu as hydrophilic amino acids)

RN 266325-39-7 HCAPLUS

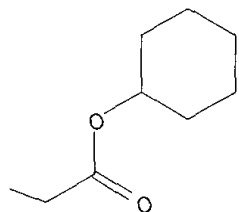
CN L-Lysine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[[2-chlorophenyl)methoxy]carbonyl]-, 1-cyclohexyl 4-(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



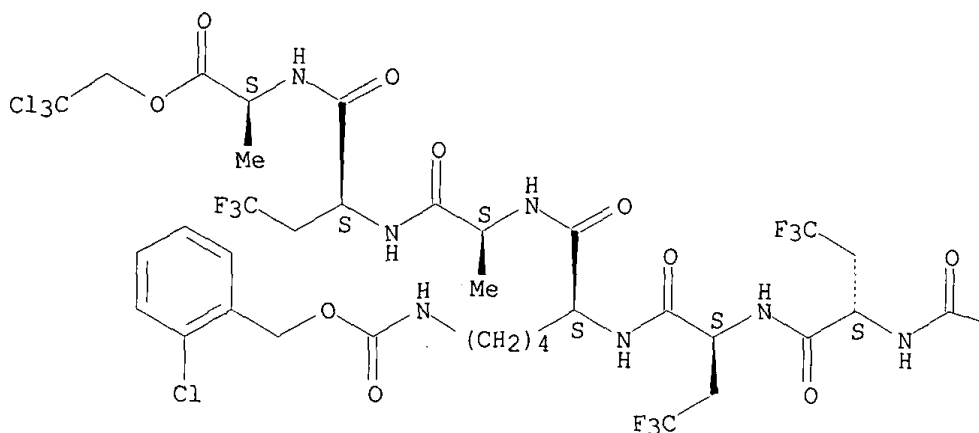
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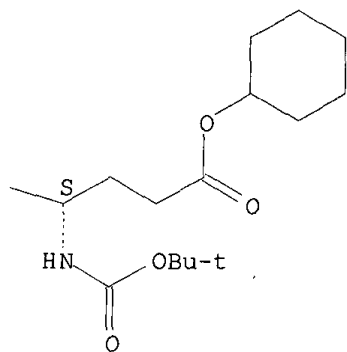
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-, 1-cyclohexyl 7-(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

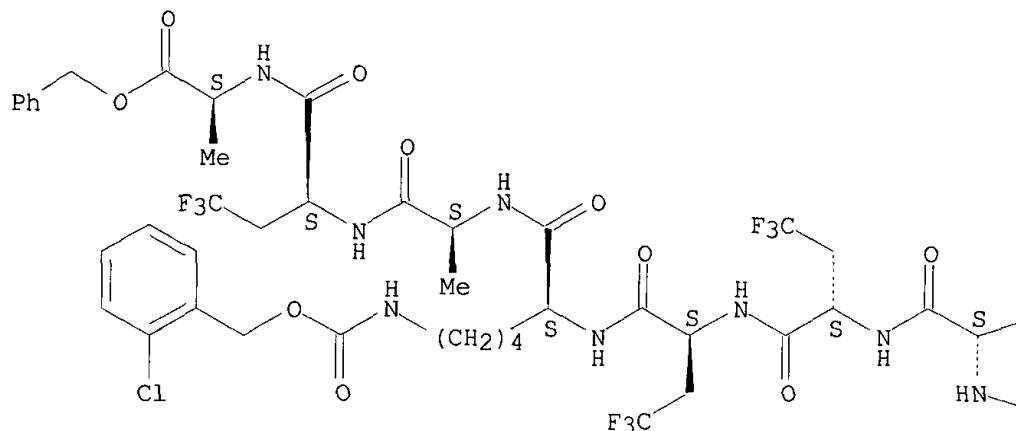


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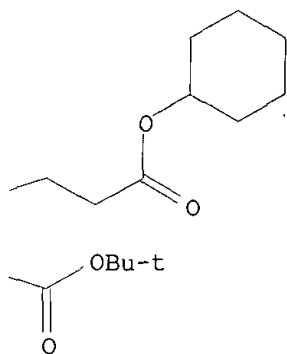
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Absolute stereochemistry.

PAGE 1-A



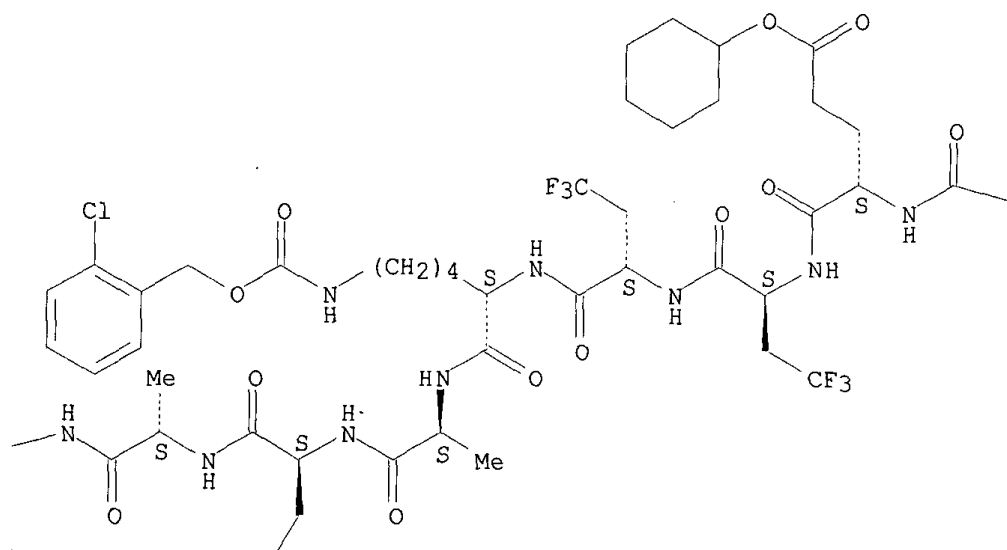
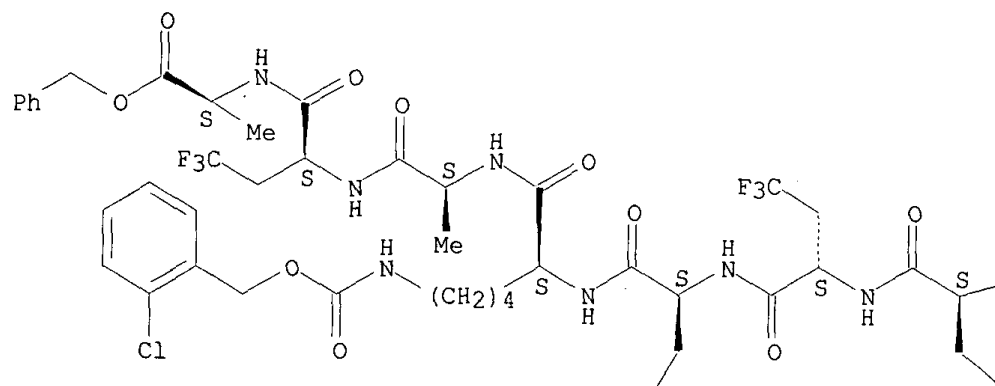
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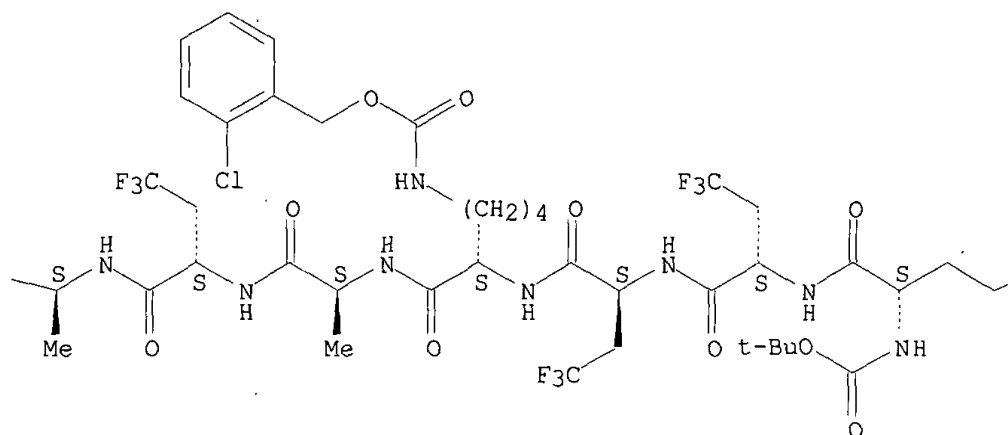
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(CA INDEX NAME)

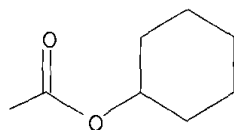
Absolute stereochemistry.



PAGE 1-C



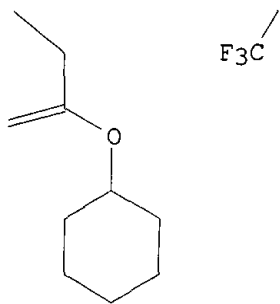
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PAGE 2-A



PAGE 2-B

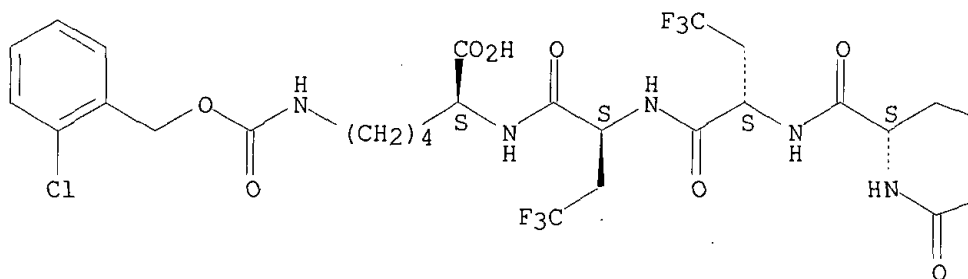


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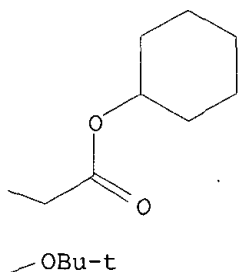
CN L-Lysine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[[(2-chlorophenyl)methoxy]carbonyl]-, 1-cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

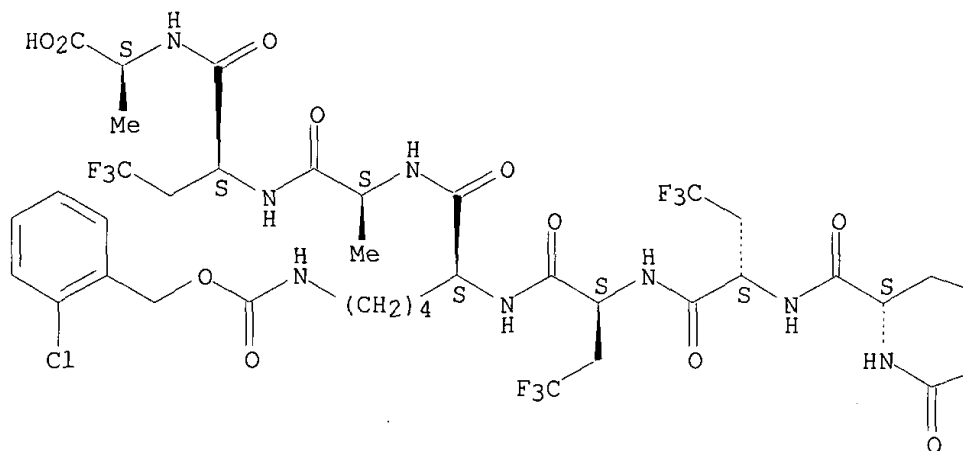


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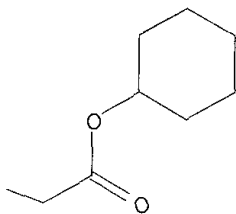
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-, 1-cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



~~_____~~ OBU-t

RN 266325-62-6 HCAPLUS

CN L-Alanine, L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-, 1-cyclohexyl 7-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

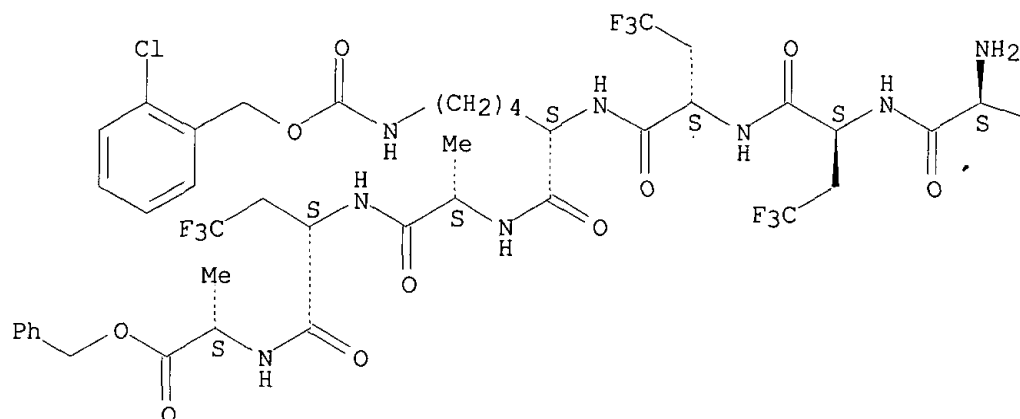
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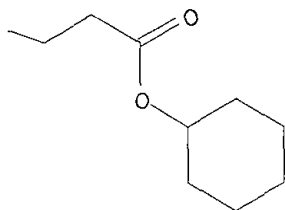
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Absolute stereochemistry.

PAGE 1-A



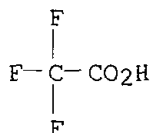
PAGE 1-B



CM 2

CRN 76-05-1

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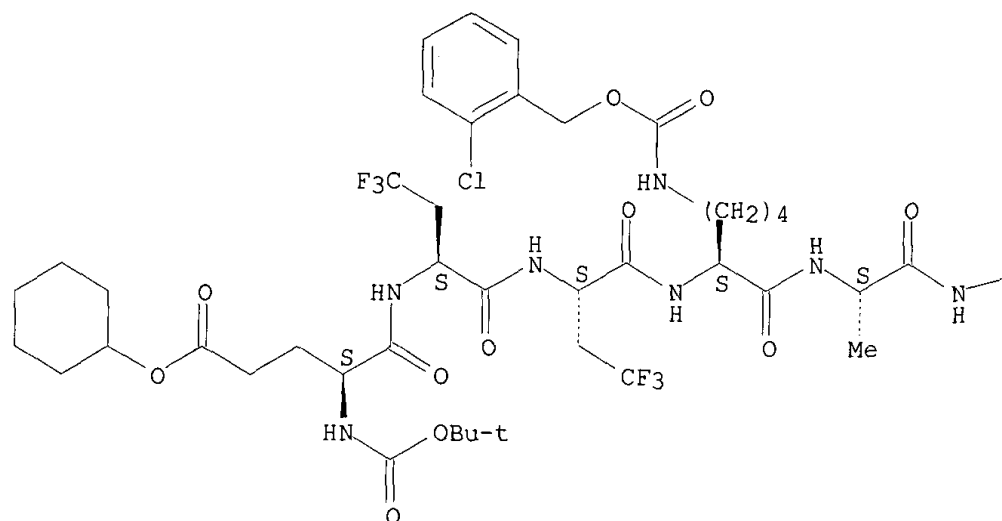


RN 266325-63-7 HCAPLUS

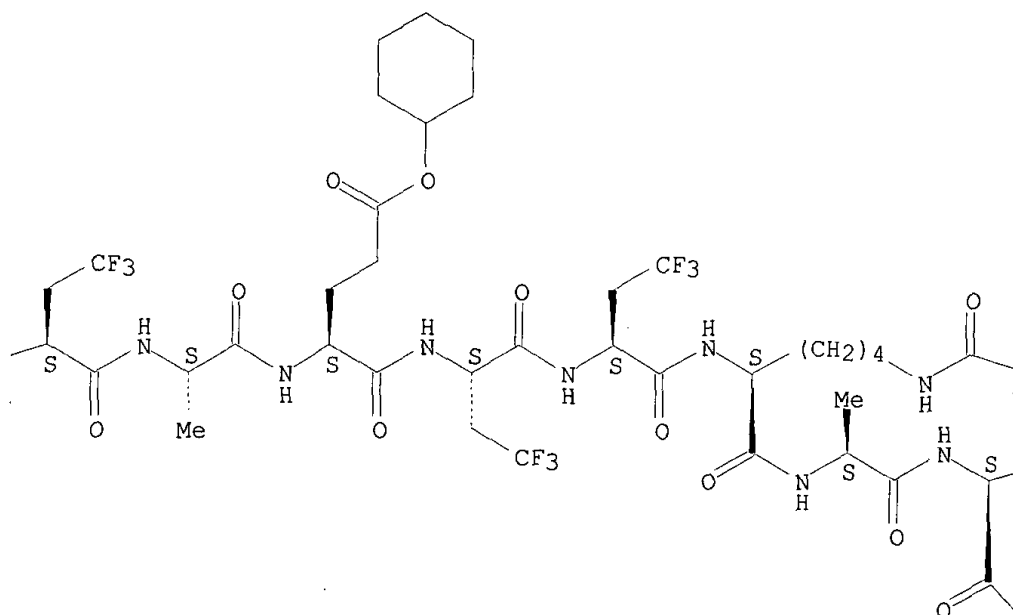
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-L-alanyl-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-, 1,8-dicyclohexyl 14-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

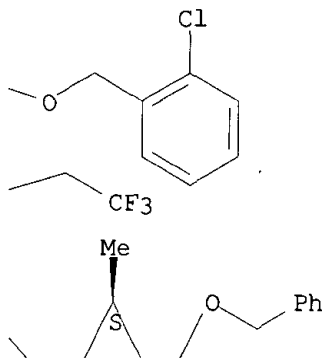
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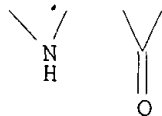
PAGE 1-B



PAGE 1-C



PAGE 2-C



RN 266325-65-9 HCAPLUS
 CN L-Alanine, L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-L-alanyl-L-.alpha.-glutamyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-alanyl-(2S)-2-amino-4,4,4-trifluorobutanoyl-, 1,8-dicyclohexyl 14-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

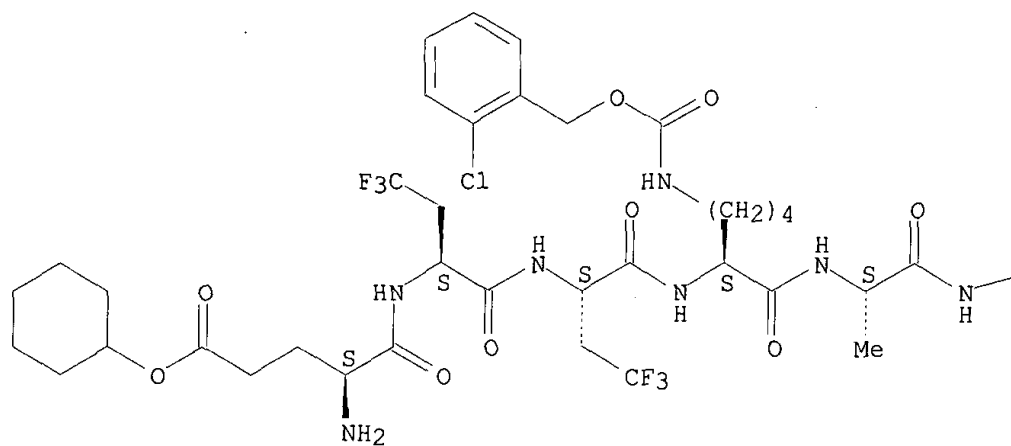
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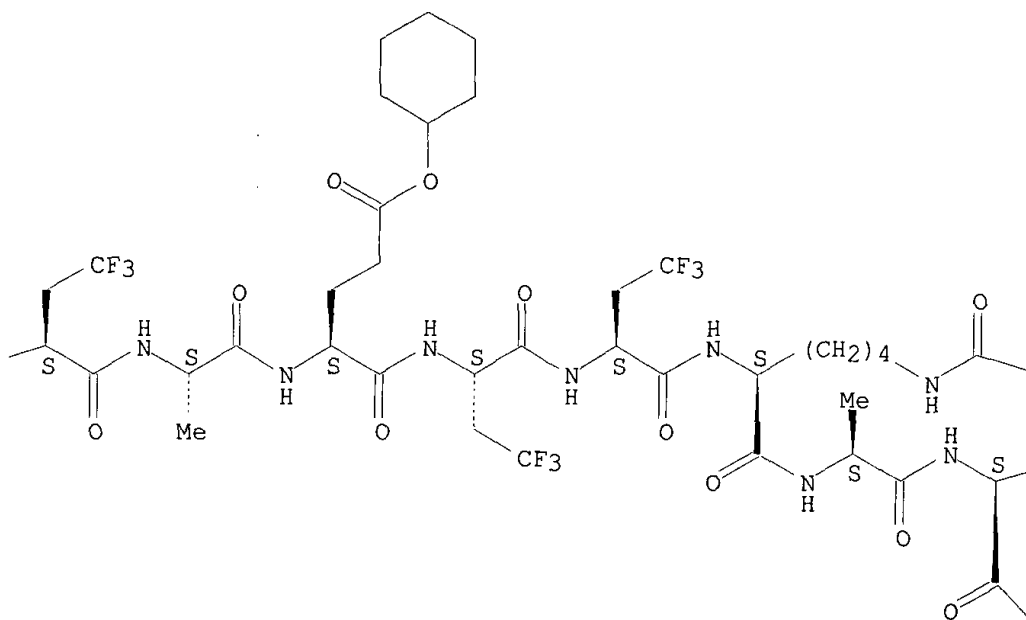
CMF C93 H120 C12 F18 N16 O23

Absolute stereochemistry.

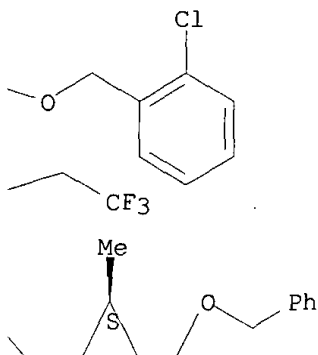
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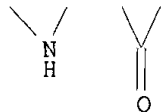
PAGE 1-B



PAGE 1-C



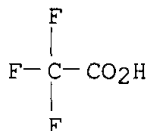
PAGE 2-C



CM 2

CRN 76-05-1

CMF C2 H F3 O2



REFERENCE COUNT:

64

THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L23 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:470226 HCAPLUS

DOCUMENT NUMBER: 131:224119

TITLE: Peptide mini-vectors for gene delivery

AUTHOR(S): Cooper, Robert G.; Harbottle, Richard P.; Schneider, Holm; Coutelle, Charles; Miller, Andrew D.

CORPORATE SOURCE: The Imperial College Genetic Therapies Centre
Department of Chemistry, Imperial College of Science,
Technology and Medicine, London, SW7 2AY, UKSOURCE: Angew. Chem., Int. Ed. (1999), 38(13/14), 1949-1952
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Described is an alternative to cationic liposome vector transfection systems based on peptides, providing one of the smallest and simplest vector systems yet reported for the delivery of nucleic acids. The system originates from the discovery that a peptide contg. a cyclic N-terminal moiety and a hexadeca(L-lysine) moiety could mediate gene delivery in vivo. The cyclic N-terminal moiety contains an Arg-Gly-Asp (RGD) peptide motif shown to interact with integrins. The peptides are expected to bind nucleic acids by means of the poly-lysine moiety and then enter cells via integrin binding and receptor-mediated endocytosis.

IT 243988-87-6 243988-88-7

RL: RCT (Reactant)

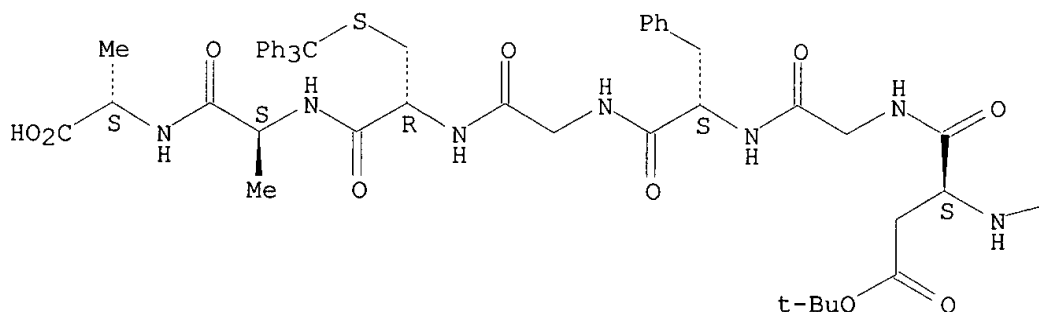
(peptide mini-vectors for gene **delivery**)

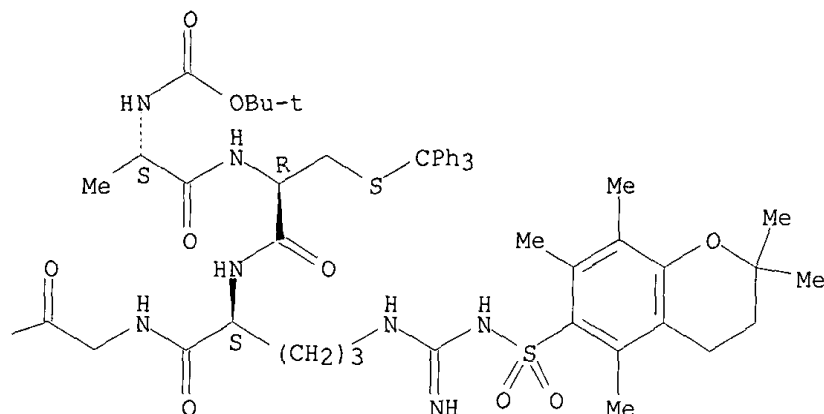
RN 243988-87-6 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-S-(triphenylmethyl)-L-cysteiny-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl-L-.alpha.-aspartylglycyl-L-phenylalanylglycyl-S-(triphenylmethyl)-L-cysteiny-L-alanyl-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

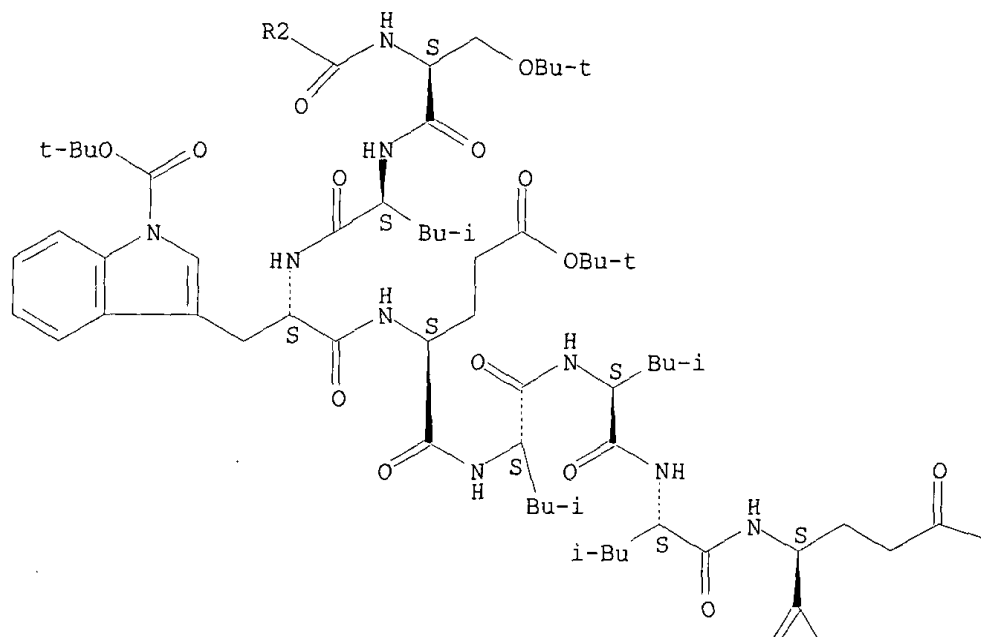




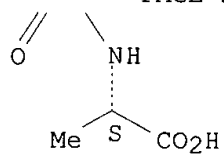
RN 243988-88-7 HCAPLUS

CN L-Alanine, glycyl-L-leucyl-L-phenylalanyl-L-α-glutamyl-L-alanyl-L-leucyl-L-leucyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-O-(1,1-dimethylethyl)-L-seryl-L-leucyl-1-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-L-α-glutamyl-L-leucyl-L-leucyl-L-α-glutamyl-, 4,8,11,15,19-pentakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

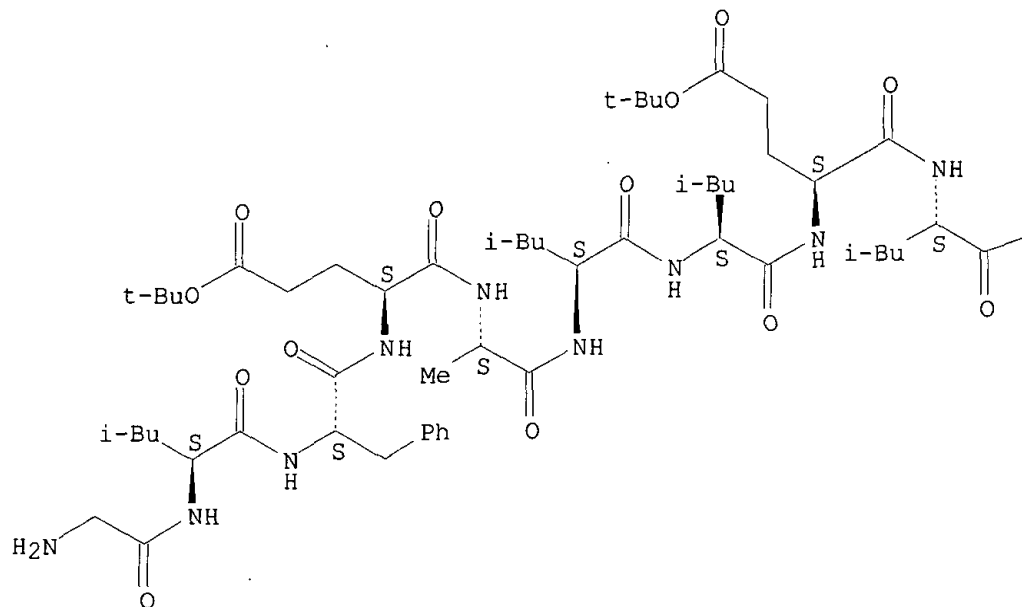
Absolute stereochemistry.



—OBu-t



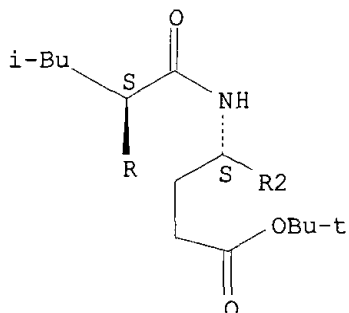
PAGE 3-A



PAGE 3-B



PAGE 4-A



REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CANELLA 09/544,644

=> d ibib abs hitstr 6

L23 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:458425 HCAPLUS
 DOCUMENT NUMBER: 132:148528
 TITLE: Technetium-99m somatostatin analogues: effect of
 labelling methods and peptide sequence
 AUTHOR(S): Decristoforo, Clemens; Mather, Stephen J.
 CORPORATE SOURCE: Nuclear Medicine Research Laboratory, St.
 Bartholomew's Hospital, West Smithfield, London, EC1A
 7BE, UK
 SOURCE: European Journal of Nuclear Medicine (1999), 26(8),
 869-876
 CODEN: EJNMD9; ISSN: 0340-6997
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB In this paper the preclin. evaluation of the somatostatin analog RC160
 labeled with technetium-99m using bifunctional chelators (BFCs) based on
 the hydrazinonicotinamide (HYNIC) and N3S system is described and a
 comparison made with [Tyr3]-octreotide (TOC). Conjugates of both peptides
 with HYNIC, and of RC160 with benzoyl-MAG3 and an N3S-adipate deriv. were
 prepd. and radiolabelling performed at high specific activities using
 tricine, tricine/nicotinic acid and ethylenediamine-N,N'-diacetic acid
 (EDDA) as co-ligands for HYNIC conjugates. All conjugates and
 99mTc-labeled peptides showed preserved binding affinity for the
 somatostatin receptor (IC50, Kd<5 nM). The biodistribution was markedly
 dependent on the BFC and co-ligand used, with the amidothiol ligands
 showing a greater degree of hepatobiliary clearance, the HYNIC/tricine
 complex higher blood levels and the HYNIC/EDDA complex the highest level
 of renal excretion and lowest blood levels. All peptide conjugates showed
 receptor-mediated uptake in tumor xenografts, but tumor uptake was
 significantly lower for the 99mTc-RC160 derivs. compared with
 99mTc-EDDA/HYNIC-[Tyr3]-octreotide (0.2%-3.5%ID/g vs 9.7%ID/g) and
 correlated well with the reduced internalization rate for RC160 derivs.
 Our results show that the selection of the labeling approach as well as
 the right choice of the peptide structure are crucial for labeling
 peptides with 99mTc to achieve complexes with favorable biodistribution.
 Despite the relatively low tumor uptake compared with 99mTc-EDDA/HYNIC-
 [Tyr3]-octreotide, 99mTc-RC160 could play a role in imaging tumors that do
 not bind octreotide derivs.

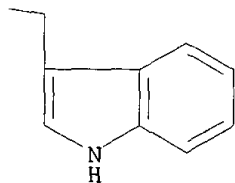
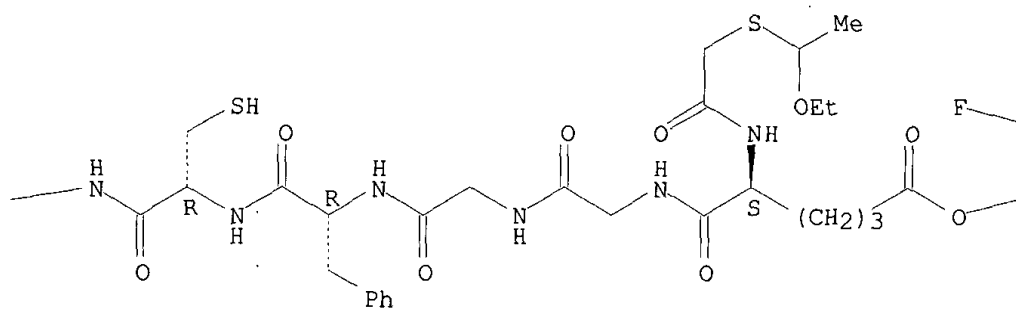
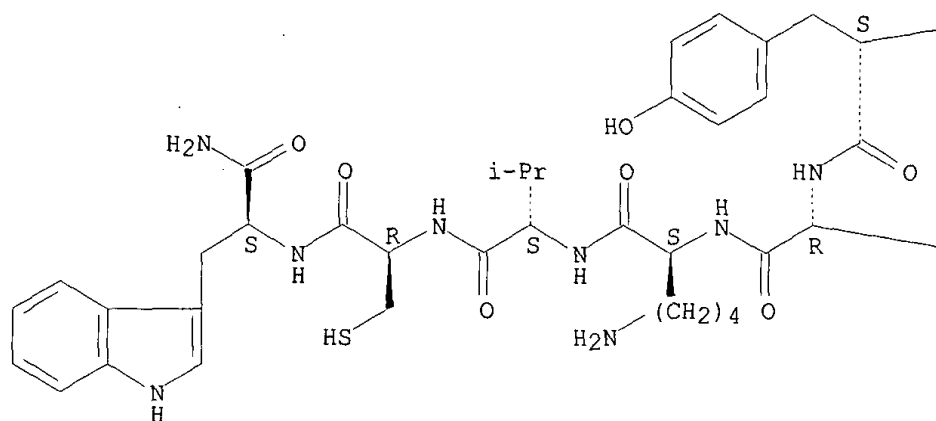
IT 257943-18-3 257943-18-3D, technetium-99 complex
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(technetium-99m complexes with somatostatin analogs: prepn.,
 biodistribution and tumor uptake)

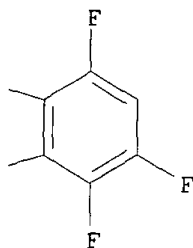
RN 257943-18-3 HCAPLUS

CN L-Tryptophanamide, N-[[[(1-ethoxyethyl)thio]acetyl]-6-oxo-6-(2,3,5,6-
 tetrafluorophenoxy)-L-norleucylglycylglycyl-D-phenylalanyl-L-cysteinyl-L-
 tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-C

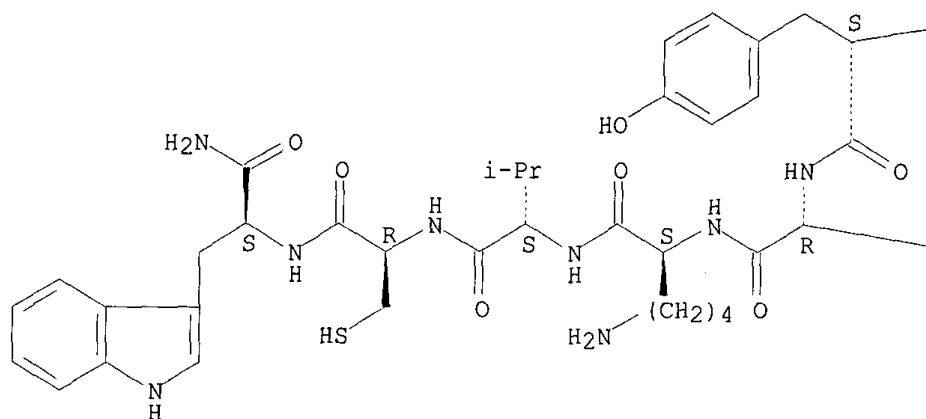


RN 257943-18-3 HCAPLUS

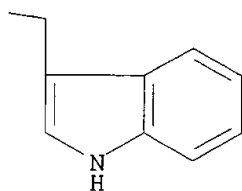
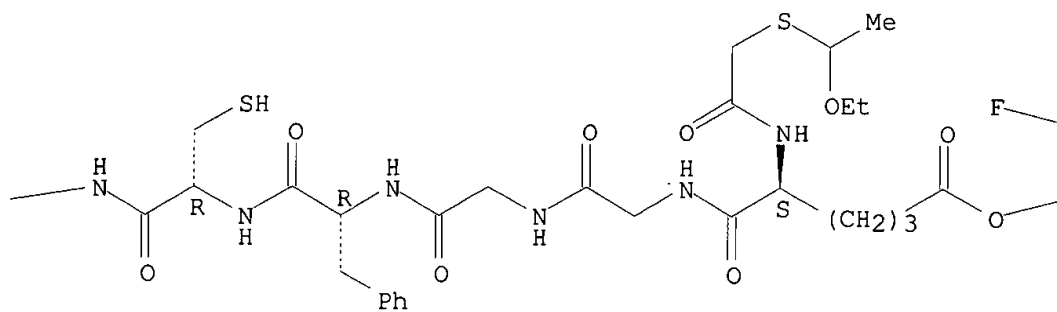
CN L-Tryptophanamide, N-[[[(1-ethoxyethyl)thio]acetyl]-6-oxo-6-(2,3,5,6-tetrafluorophenoxy)-L-norleucylglycylglycyl-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

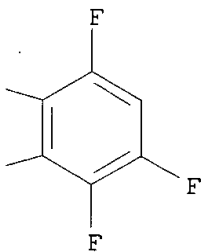
PAGE 1-A



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PAGE 1-C



REFERENCE COUNT:

21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 7

L23 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:12213 HCAPLUS

DOCUMENT NUMBER: 130:81892

TITLE: Preparation of therapeutic delivery using compounds
self-assembled into high axial ratio microstructures

INVENTOR(S): Yager, Paul; Gelb, Michael H.; Carlson, Paul A.; Lee,
Kyu-jin C.; Lukyanov, Anatoly N.; Goldstein, Alex S.

PATENT ASSIGNEE(S): University of Washington, USA

SOURCE: U.S., 26 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5851536 | A | 19981222 | US 1996-752848 | 19961121 |
| US 6180114 | B1 | 20010130 | US 1998-219057 | 19981222 |
| PRIORITY APPLN. INFO.: | | | US 1996-752848 | A2 19961121 |
| | | | US 1998-87179P | P 19980529 |

AB Therapeutic agents HARFM-Th or HARFM-S-Th (HARFM = high axial ratio forming material; Th = therapeutic agent; S = spacer group) were prepd. as therapeutic delivery agents. Thus, Gly-L-Lys-Sar-L-Pro-L-Glu[NH(CH₂)₁₁CH₃]₂ was prepd. via coupling the glutamine lipid with the corresponding diprotected peptide. Release of the therapeutic by the agent generally follows either 0-order kinetics or pseudo first order kinetics. A method for delivering drugs to animals or persons also was described. The method comprises administering an effective amt. of a therapeutic self-assembled into an HAR microstructure to the animal or person.

IT 218782-35-5P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of therapeutic **delivery** using compds. self-assembled into high axial ratio microstructures)

RN 218782-35-5 HCAPLUS

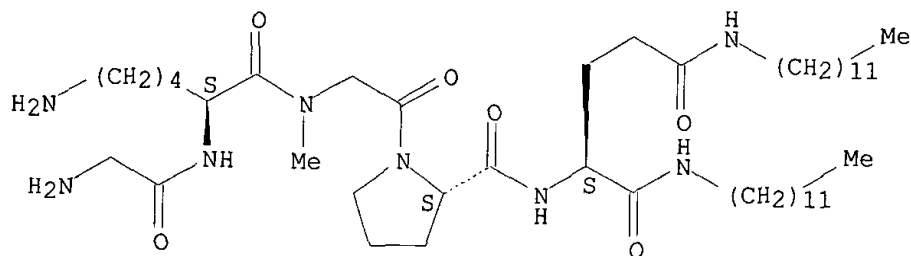
CN L-Glutamamide, glycyl-L-lysyl-N-methylglycyl-L-prolyl-N₁,N₅-didodecyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 191354-73-1

CMF C45 H86 N8 O6

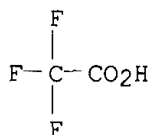
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 191354-73-1P 191354-82-2P 191354-83-3P

191354-89-9P 218782-41-3P

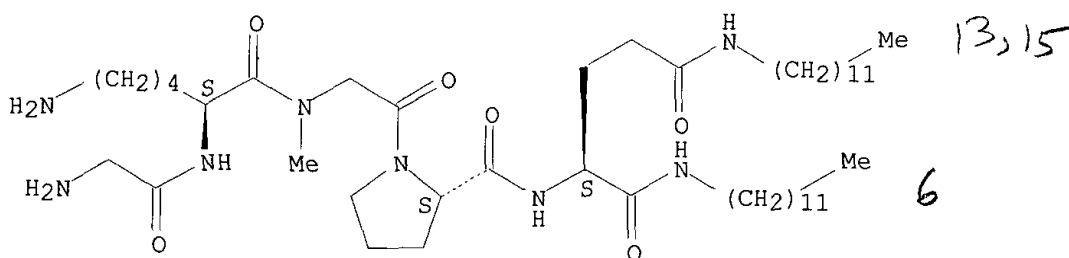
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of therapeutic **delivery** using compds. self-assembled into high axial ratio microstructures)

RN 191354-73-1 HCAPLUS

CN L-Glutamamide, glycyl-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 191354-82-2 HCAPLUS

CN L-Glutamamide, N-acetylglycyl-L-arginyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

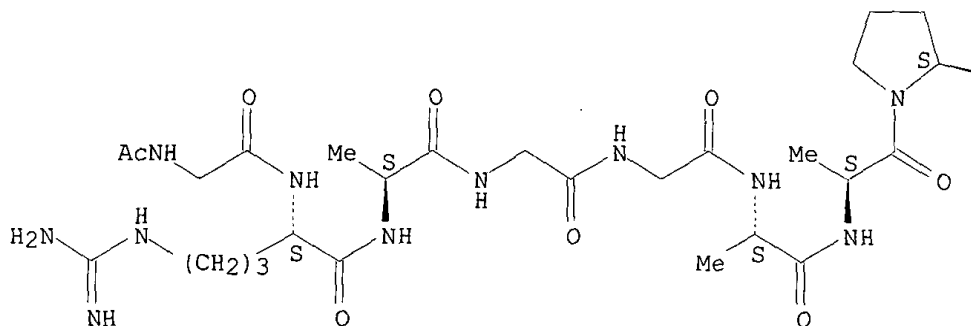
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CRN 191354-81-1

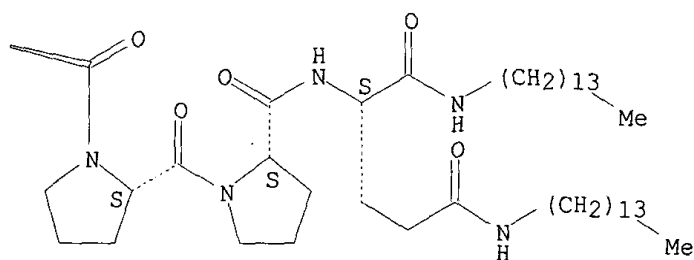
CMF C71 H126 N16 O13

Absolute stereochemistry.

PAGE 1-A



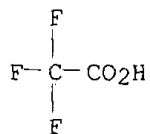
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CRN 76-05-1

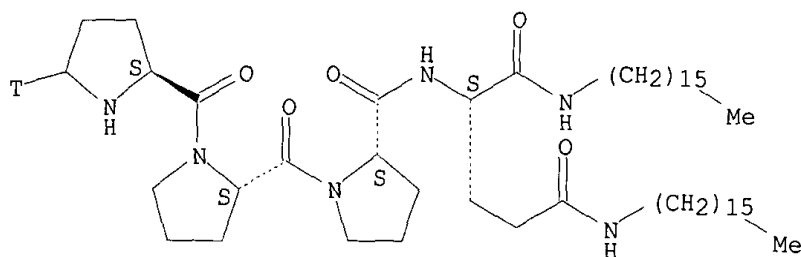
CMF C2 H F3 O2



RN 191354-83-3 HCAPLUS

CN L-Glutamamide, L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl-,
monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

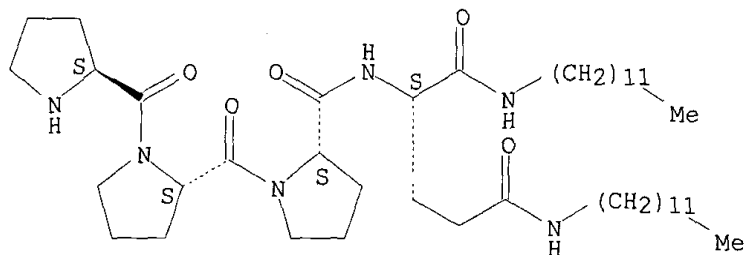


● HCl

RN 191354-89-9 HCAPLUS

CN L-Glutamamide, L-prolyl-L-prolyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

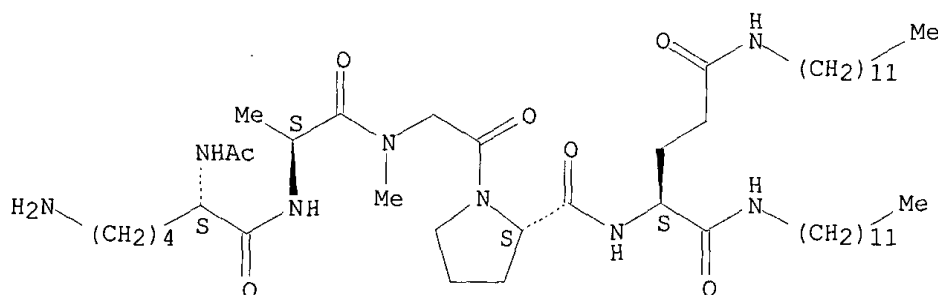
Absolute stereochemistry.



RN 218782-41-3 HCAPLUS

CN L-Glutamamide, N2-acetyl-L-lysyl-L-alanyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 128701-85-9P 191354-80-0P 191354-87-7P

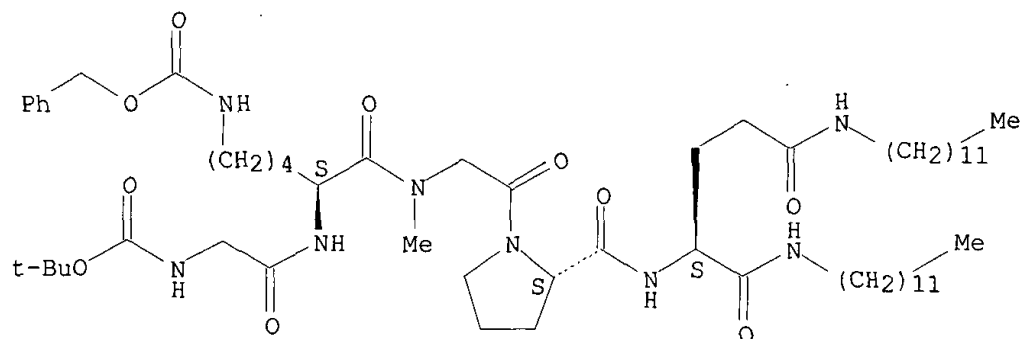
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of therapeutic **delivery** using compds. self-assembled
 into high axial ratio microstructures)

RN 128701-85-9 HCAPLUS

CN L-Glutamamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N6-
 [(phenylmethoxy)carbonyl]-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

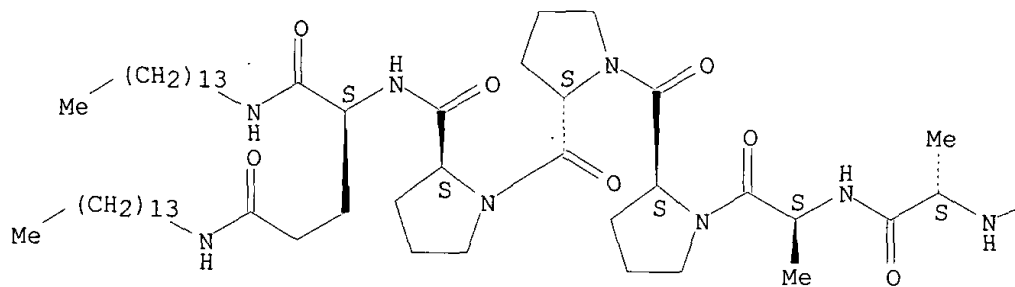


RN 191354-80-0 HCAPLUS

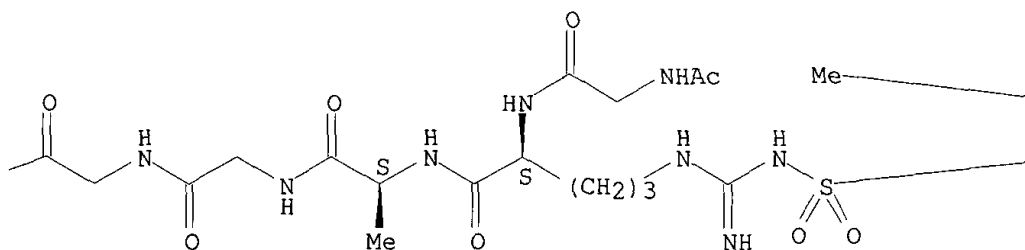
CN L-Glutamamide, N-acetylglycyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl) sulfonyl]amino]iminomethyl]-L-ornithyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl- (9CI) (CA INDEX NAME)

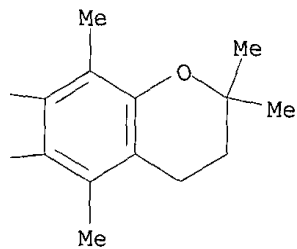
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

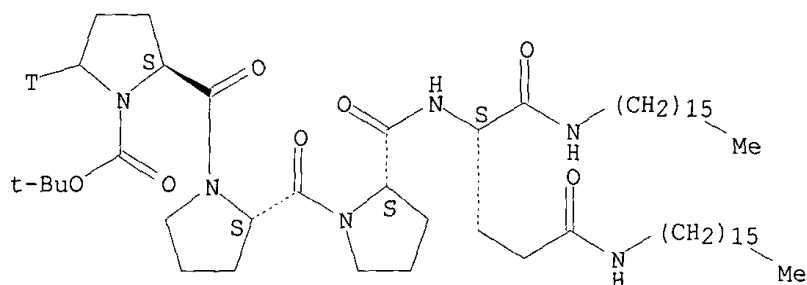




RN 191354-87-7 HCAPLUS

CN L-Glutamamide, 1-[(1,1-dimethylethoxy)carbonyl]-L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L23 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:448098 HCAPLUS
 DOCUMENT NUMBER: 127:70860
 TITLE: Therapeutic delivery using compounds self-assembled
 into high-axial-ratio microstructures
 INVENTOR(S): Yager, Paul; Gelb, Michael H.; Carlson, Paul A.;
 Lukyanov, Anatoly N.; Goldstein, Alex S.; Lee, Kyujin
 C.
 PATENT ASSIGNEE(S): University of Washington, USA
 SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

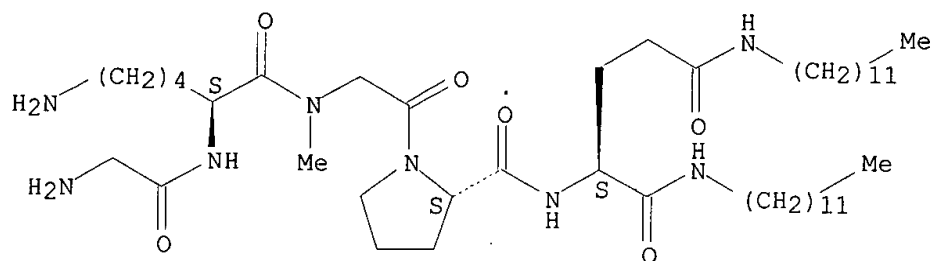
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9718840 | A2 | 19970529 | WO 1996-US18850 | 19961121 |
| WO 9718840 | A3 | 19971009 | | |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9712738 | A1 | 19970611 | AU 1997-12738 | 19961121 |
| PRIORITY APPLN. INFO.: | | | US 1995-25137 | 19951122 |
| | | | WO 1996-US18850 | 19961121 |

AB Therapeutic agents comprising plural therapeutic compds. self-assembled into high-axial-ratio microstructures such as tubules, cochleate cylinders, helical ribbons, and twisted ribbons are described. A therapeutic compd. may alternatively be coupled to an agent forming such microstructures, directly or through an enzymically cleavable spacer, for delivery of the drug to an animal. High-axial-ratio microstructure-forming agents include glutamate- or polyglutamate-based amphiphiles, phosphatidylcholines with tricosadiynoyl fatty acyl chains, and fatty acyl galactocerebrosides. Release of the therapeutic compd. by the conjugate generally follows either zero-order or pseudo-1st-order kinetics. Synthesis of some self-assembling glutamine-based lipids and ceramides is described.

IT 191354-73-1P 191354-81-1P 191354-82-2P
 191354-83-3P 191354-89-9P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (therapeutic **delivery** using compds. self-assembled into high-axial-ratio microstructures)

RN 191354-73-1 HCAPLUS
 CN L-Glutamamide, glycyl-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

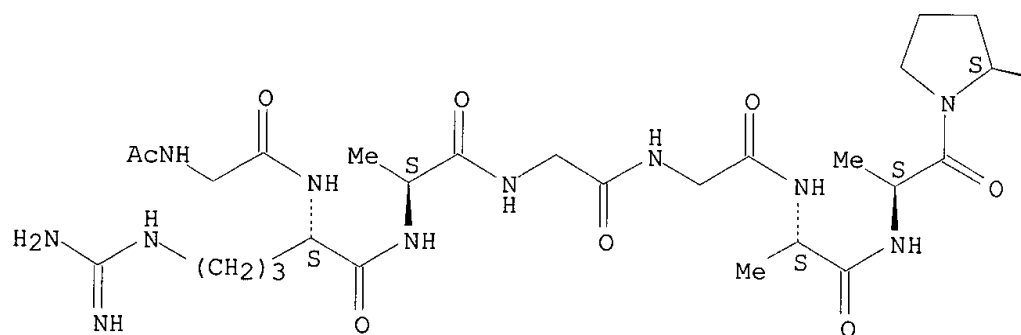


RN 191354-81-1 HCAPLUS

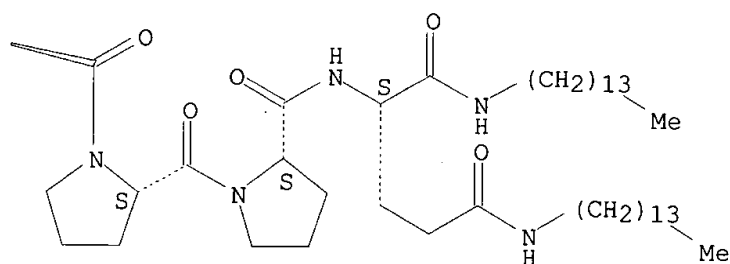
CN L-Glutamamide, N-acetylglycyl-L-arginyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 191354-82-2 HCAPLUS

CN L-Glutamamide, N-acetylglycyl-L-arginyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

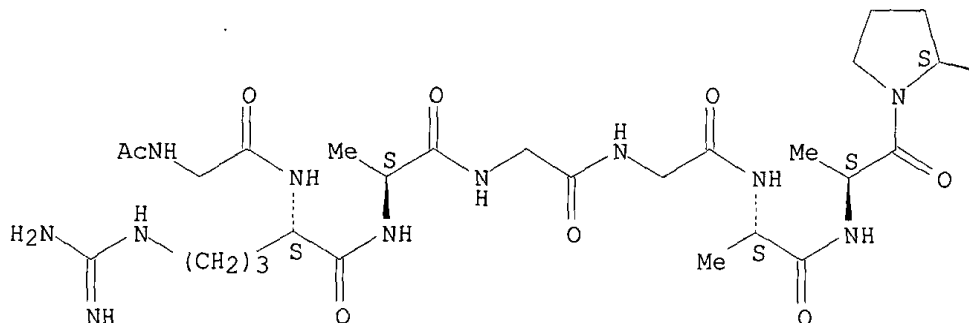
CM 1

CRN 191354-81-1

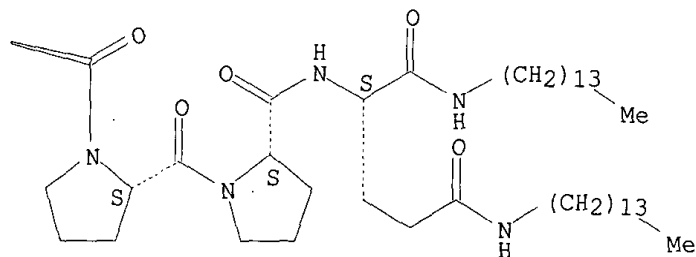
CMF C71 H126 N16 O13

Absolute stereochemistry.

PAGE 1-A



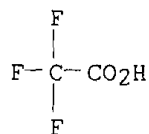
PAGE 1-B



CM 2

CRN 76-05-1

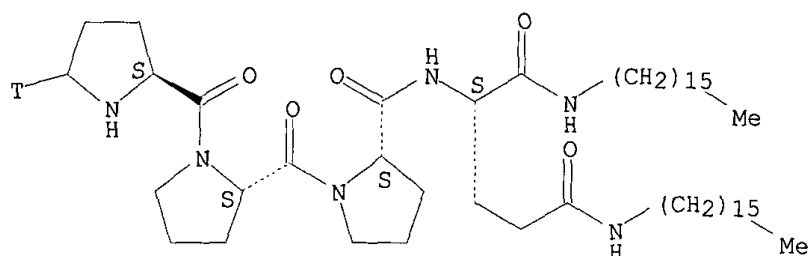
CMF C2 H F3 O2



RN 191354-83-3 HCAPLUS

CN L-Glutamamide, L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

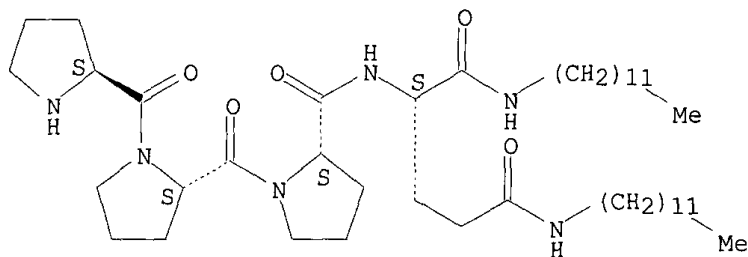


● HCl

RN 191354-89-9 HCAPLUS

CN L-Glutamamide, L-prolyl-L-prolyl-L-prolyl-N1,N5-didodecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 191354-80-0

RL: RCT (Reactant)

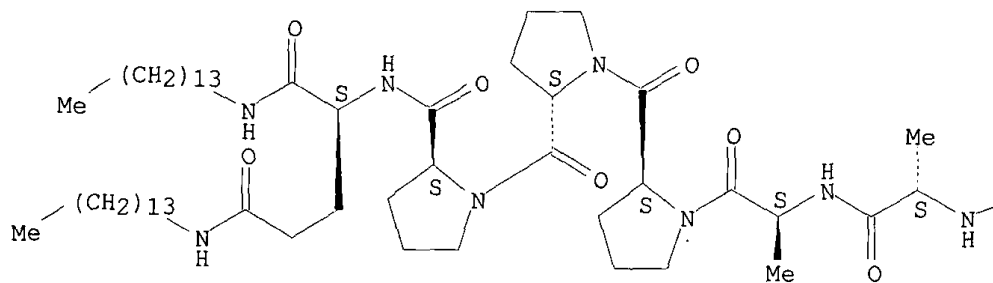
(therapeutic **delivery** using compds. self-assembled into high-axial-ratio microstructures)

RN 191354-80-0 HCAPLUS

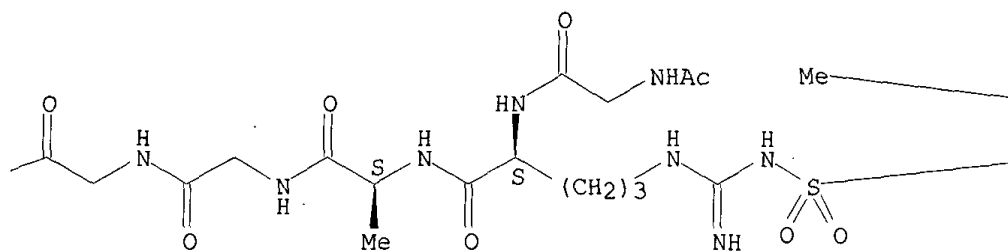
CN L-Glutamamide, N-acetylglycyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-alanylglycylglycyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-prolyl-N1,N5-ditetradecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

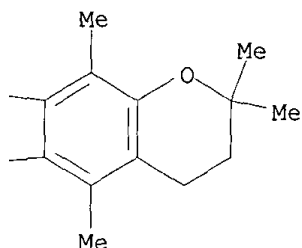
PAGE 1-A



PAGE 1-B



PAGE 1-C



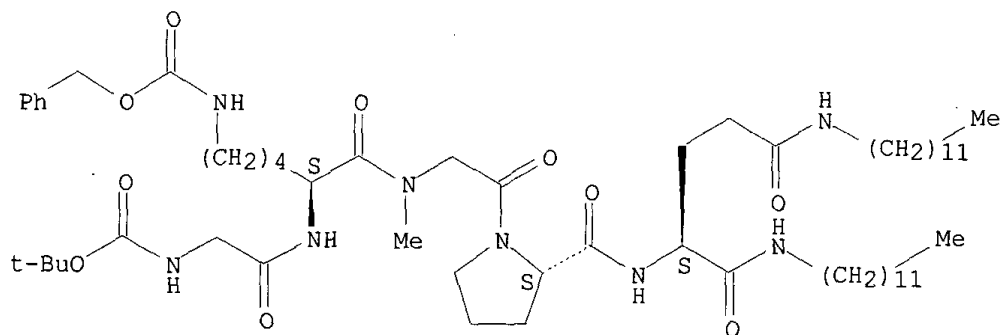
IT 128701-85-9P 191354-72-0P 191354-87-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (therapeutic **delivery** using compds. self-assembled into
 high-axial-ratio microstructures)

RN 128701-85-9 HCAPLUS

CN L-Glutamamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N6-
 [(phenylmethoxy)carbonyl]-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl-
 (9CI) (CA INDEX NAME)

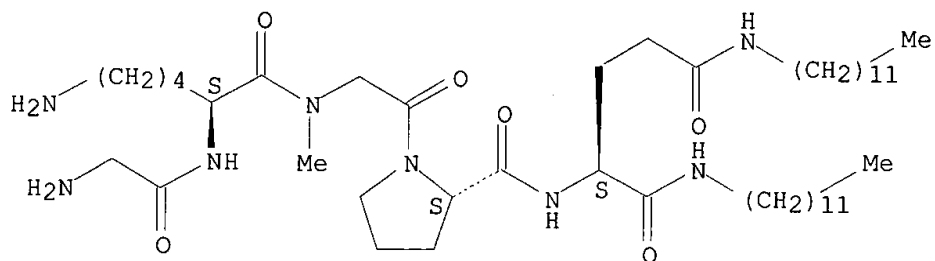
Absolute stereochemistry.



RN 191354-72-0 HCAPLUS

CN L-Glutamamide, glycyl-L-lysyl-N-methylglycyl-L-prolyl-N1,N5-didodecyl-,
 hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

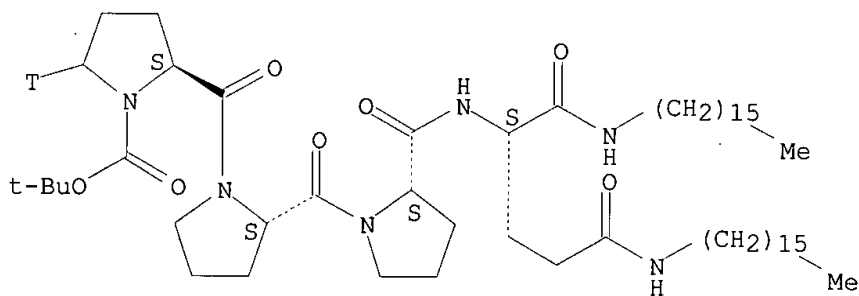


● x HCl

RN 191354-87-7 HCAPLUS

CN L-Glutamamide, 1-[(1,1-dimethylethoxy)carbonyl]-L-prolyl-5-t-L-prolyl-L-prolyl-N1,N5-dihexadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 9

L23 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:299434 HCAPLUS

DOCUMENT NUMBER: 126:347220

TITLE: Peptide Targeting and Delivery across the Blood-Brain Barrier Utilizing Synthetic Triglyceride Esters: Design, Synthesis, and Bioactivity

AUTHOR(S): Patel, Dinesh; McKinley, Brian D.; Davis, Thomas P.; Porreca, Frank; Yamamura, Henry I.; Hruby, Victor J.

CORPORATE SOURCE: Departments of Chemistry and Pharmacology, University of Arizona, Tucson, AZ, 85721, USA

SOURCE: Bioconjugate Chem. (1997), 8(3), 434-441

CODEN: BCCHE; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As an approach to the development of therapeutically useful peptide pharmaceuticals that can penetrate the blood-brain barrier, we have designed and demonstrated the application of a carrier-targeting system. We have developed a prodrug design strategy that is designed to utilize membrane-bound enzymes whereby release of a bioactive peptide from a highly lipophilic triglyceride peptide-carrier is achieved in situ, thus attaining high localized concns. of the bioactive peptide. Following localization of such a system, normal peptidase and lipase action is utilized to release the active peptide (deltorphin II) intact and in high concn. At present, the exact mechanisms are unclear, but the obsd. results in which analgesia is obsd. following peripheral administration suggest that the active peptide is able to cross the blood-brain barrier and sustain prolonged periods of analgesia as detd. by antinociception tests by release of the bioactive peptide. In vitro tests of binding and bioactivity by the peptide conjugate show essentially no potency in either target or control analogs, but potent antinociceptive effects are obsd. following peripheral administration.

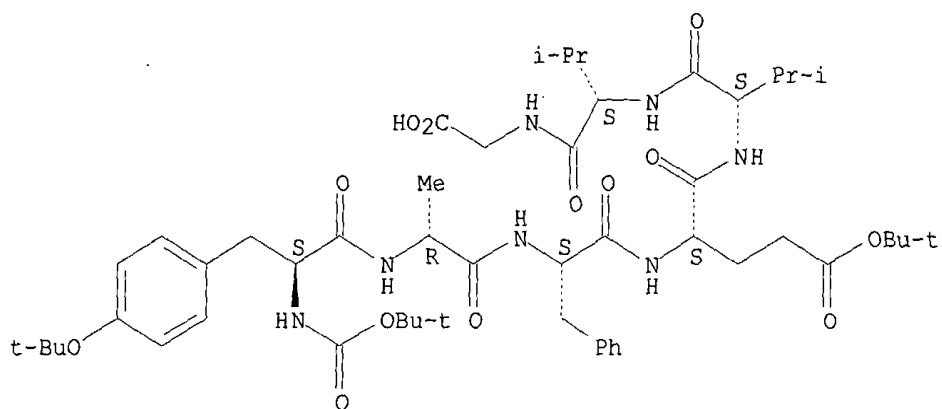
IT 189625-55-6P 189625-57-8P 189625-62-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (peptide targeting and **delivery** across the blood-brain
 barrier utilizing synthetic triglyceride esters)

RN 189625-55-6 HCAPLUS

CN Deltorphin B, 1-[N-[(1,1-dimethylethoxy)carbonyl]-O-(1,1-dimethylethyl)-L-tyrosine]-7-glycine-, 4-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

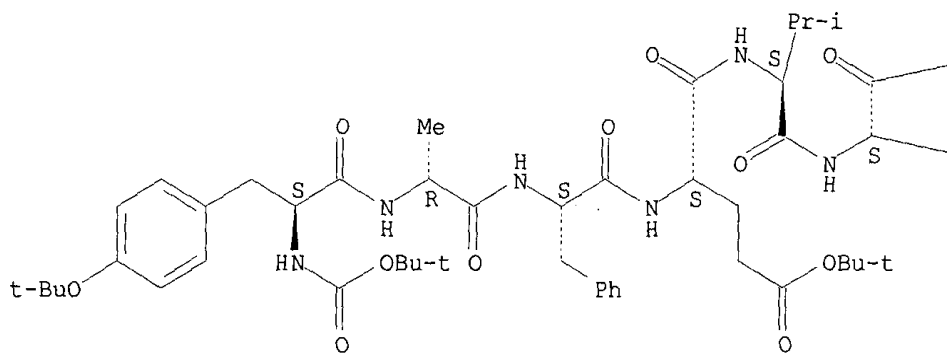


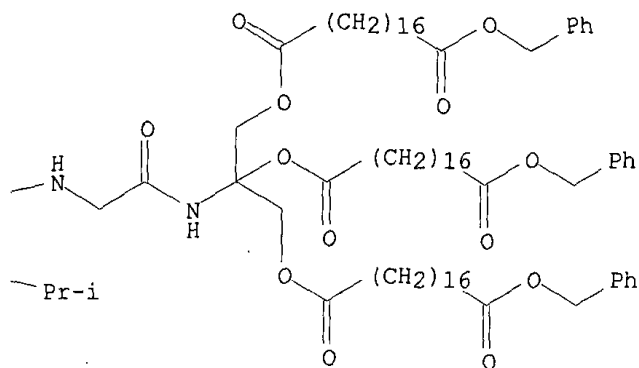
RN 189625-57-8 HCAPLUS

CN Deltorphen B, 1-[N-[(1,1-dimethylethoxy)carbonyl]-O-(1,1-dimethylethyl)-L-tyrosine]-7-[N-[1,2-bis[[1,18-dioxo-18-(phenylmethoxy)octadecyl]oxy]-1-[[[1,18-dioxo-18-(phenylmethoxy)octadecyl]oxy]methyl]ethyl]glycinamide]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

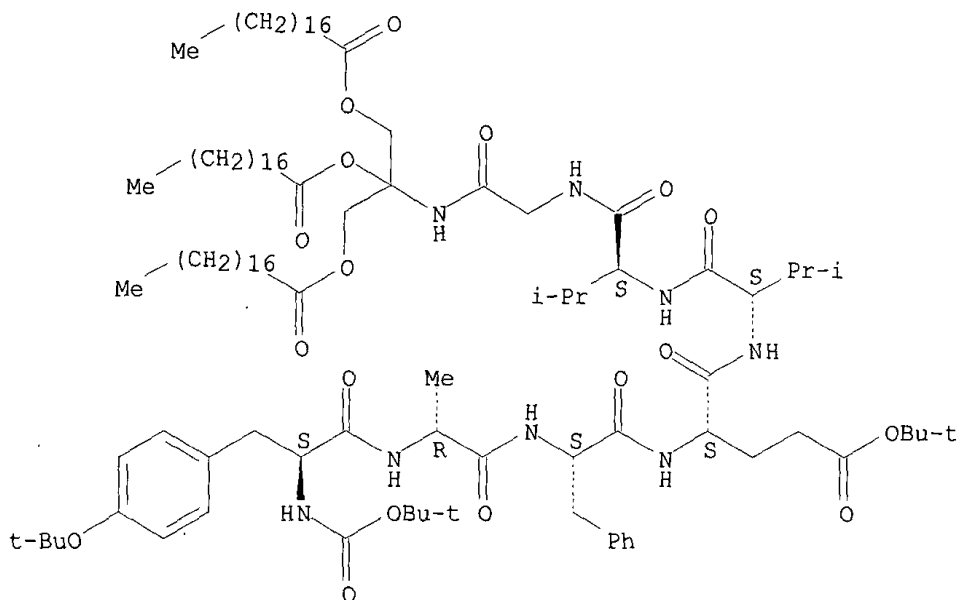




RN 189625-62-5 HCAPLUS

CN Deltorphen B, 1-[N-[(1,1-dimethylethoxy)carbonyl]-O-(1,1-dimethylethyl)-L-tyrosine]-7-[N-[1,2-bis[(1-oxooctadecyl)oxy]-1-[[[1-oxooctadecyl)oxy)methyl]ethyl]glycinamide]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 10

L23 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:678152 HCAPLUS

DOCUMENT NUMBER: 126:4284

TITLE: Lipoconjugates: structure-activity studies for pheromone analogs of *Ustilago maydis* with varied **lipophilicity**

AUTHOR(S): Koppitz, M.; Spellig, T.; Kahmann, R.; Kessler, H.

CORPORATE SOURCE: Institute Organic Chemistry & Biochemistry, Technical Univ. Munich, Garching, Germany

SOURCE: Int. J. Pept. Protein Res. (1996), 48(4), 377-390

CODEN: IJPPC3; ISSN: 0367-8377

PUBLISHER: Munksgaard

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis, biol. activities and conformational behavior of a variety of analogs of the mating pheromones of the basidiomycete *U. maydis* are reported. The pheromone analogs derived from the two allelic forms H-G-R-D-N-G-S-P-I-G-Y-S-S-Xaa-Z and H-N-R-G-Q-P-G-Y-Y-Xaa-Z, with Xaa-Z being an unidentified **lipophilic** cysteine deriv., all differ in the C-terminal residue and include -Cys(farnesyl)-OMe, -Cys(farnesyl)-OH, -Cys(prenyl)-OMe, -Cys-OMe, -Cys(n-dodecyl)-OMe and the unnatural residues -Ahds-OMe (Ahds=.chi.-aminohexadecanoic acid), -Ahds-OH, -Ads-OMe (Ads = .chi.-aminodecanoic acid) and -N-Hdg-OMe (N-Hdg = N-hexadecylglycine). The synthesis of the unnatural Me ester analogs was carried out by condensation of the fully protected fragments Fmoc-G-R(Pmc)-D(tBu)-N(Trt)-G-S(tBu)-P-I-G-Y(tBu)-S(tBu)-OH (I) and Fmoc-N(Trt)-R(Pmc)-G-Q(Trt)-P-G-Y(tBu)-Y(tBu)-OH (II), resp., prepd. by Fmoc-SPPS, with the appropriate Me ester compds. and subsequent deprotection with TFA/scavenger and piperidine. Synthesis and physicochem. properties of the unnatural **lipophilic** amino acid Me esters are described. The prepn. of the cysteine analogs was performed by condensation of I or II with H-Cys(Trt)-OMe and subsequent deprotection with TFA/scavenger. Alkylation of the thiol function and Fmoc-deprotection was achieved in a novel 1-pot reaction by treatment with alkyl bromide and DIPEA, quenching with EDT, and Fmoc removal by addn. of 20% piperidine. Hydrolysis of the Me esters was carried out by treatment with NaOH in MeOH/H₂O. The results of the biol. assay reveal an increase in activity with increasing chain length of the **lipophilic** anchor, with alkyl being better than prenyl and S not being essential, while the position of the anchor is optimal at C.chi. and the Me ester moiety is important. NMR studies of 2 chosen analogs in DMSO and SDS/water demonstrate that the **lipophilic** C-terminal residue has no influence on the structural behavior of the peptides. Chem.-shift and NOE patterns indicate a main all-trans conformation of the peptide backbone and a weakly populated cis conformation around the Xaa-Pro peptide bond in all 8 cases without formation of a defined folded structure. No evidence is seen that the membrane-simulating system SDS/water has a structure-inducing effect on the bound peptide. Therefore, the lipomodification in mating pheromones of *U. maydis* apparently acts to increase the effective concn. of the drug in the target cell membrane without addnl. structure-inducing or receptor-binding effects.

IT 183441-58-9P

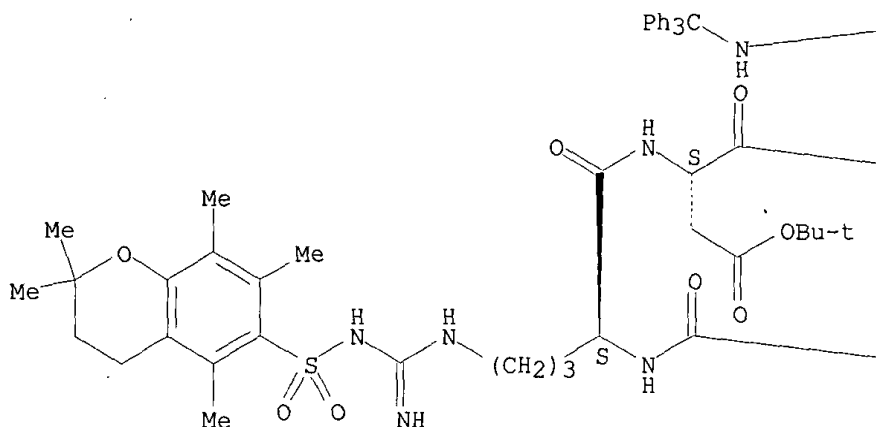
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. by solid-state synthesis and condensation reaction with Me esters synthesis of pheromone **lipoconjugate** analogs of *Ustilago maydis*)

RN 183441-58-9 HCAPLUS

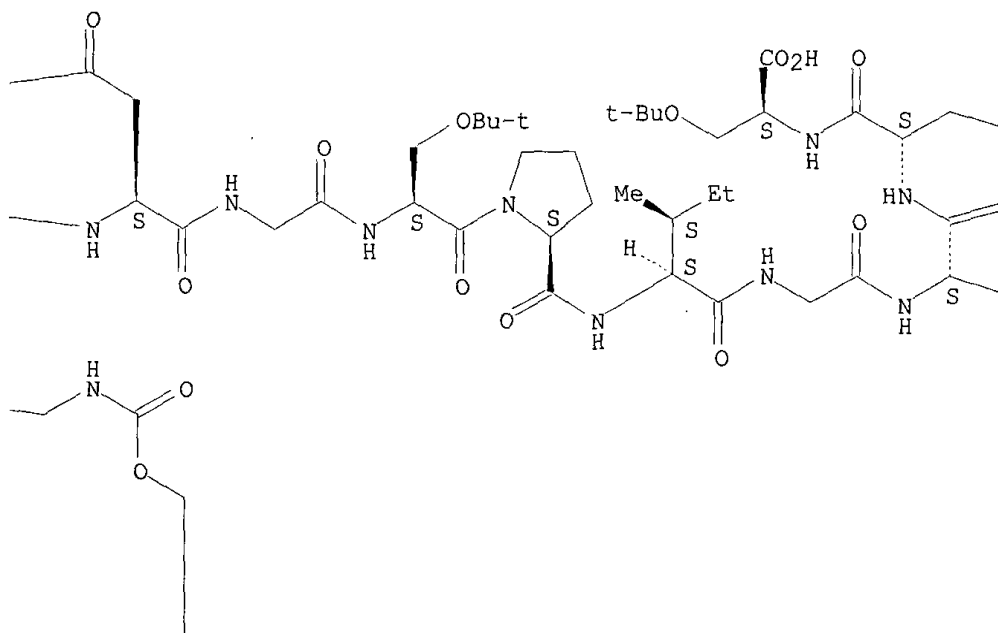
CN L-Serine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-.alpha.-aspartyl-N-(triphenylmethyl)-L-asparaginylglycyl-O-(1,1-dimethylethyl)-L-seryl-L-prolyl-L-isoleucylglycyl-O-(1,1-dimethylethyl)-L-tyrosyl-O-(1,1-dimethylethyl)-L-seryl-O-(1,1-dimethylethyl)-, 3-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

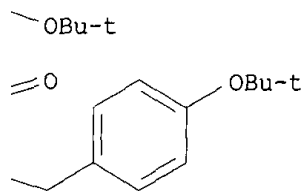
PAGE 1-A



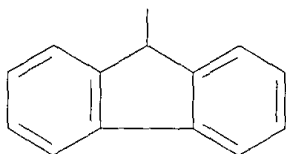
PAGE 1-B



PAGE 1-C



PAGE 2-B



=> d ibib abs hitstr 11

L23 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:668663 HCAPLUS

DOCUMENT NUMBER: 123:340850

TITLE: Non-linear hydrophobic-induced pKa shifts:
implications for efficiency of conversion to chemical energyAUTHOR(S): Urry, Dan W.; Gowda, D. Channe; Peng, Shao Qing;
Parker, Timothy M.CORPORATE SOURCE: Laboratory of Molecular Biophysics, The University of
Alabama at Birmingham, VH300, Birmingham, AL,
35294-0019, USA

SOURCE: Chem. Phys. Lett. (1995), 239(1,2,3), 67-74

CODEN: CHPLBC; ISSN: 0009-2614

DOCUMENT TYPE: Journal

LANGUAGE: English

AB By using one Asp or one Glu per thirty residues in a polytricosapeptide capable of exhibiting a hydrophobic folding and assembly transition and stepwise converting a set of the five Val residues (most proximal to the Asp or Glu residue) to more-hydrophobic Phe residues, a non-linear hydrophobic-induced pKa shift was obsd. with a .DELTA.pKa of 0.4 (Asp) and 0.3 (Glu) on addn. of 2 Phe residues per 30mer but with a .DELTA.pKa of 4.7 (Asp) and 2.7 (Glu) on going from 4 Phe/30mer to 5 Phe/30mer. As a shift in pKa can be equiv. to the conversion to chem. energy from whatever energy input (mech., chem., electrochem., pressure or light) which effects a change in hydrophobicity, the non-linear hydrophobic-induced pKa shift means increased efficiency of energy conversion with increased hydrophobicity of the protein-based polymer.

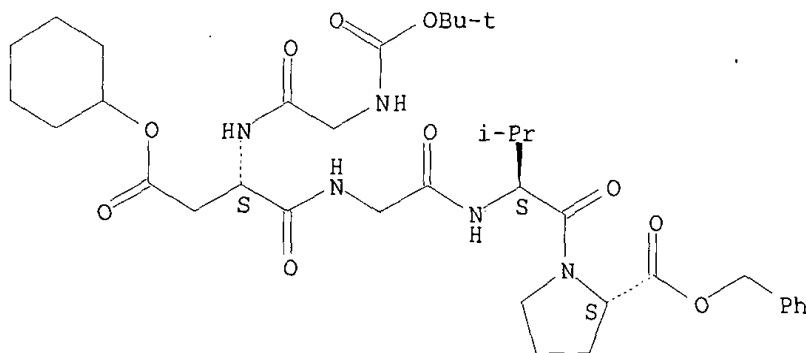
IT 170742-56-0P 170742-57-1P 170742-60-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of polytricosapeptides, their non-linear **hydrophobic**
-induced pKa shifts, and implications for efficiency of conversion to
chem. energy)

RN 170742-56-0 HCAPLUS

CN L-Proline, 1-[N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-.alpha.-
aspartyl]glycyl]-L-valyl]-, 4-cyclohexyl 2-(phenylmethyl) ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

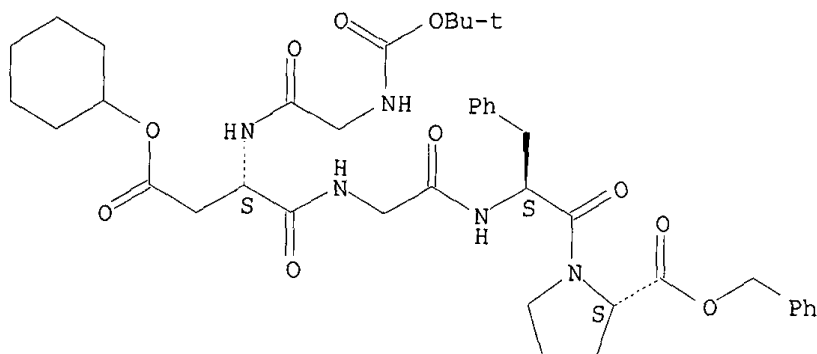


RN 170742-57-1 HCAPLUS

CN L-Proline, 1-[N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-.alpha.-
aspartyl]glycyl]-L-phenylalanyl]-, 4-cyclohexyl 2-(phenylmethyl) ester

(9CI) (CA INDEX NAME)

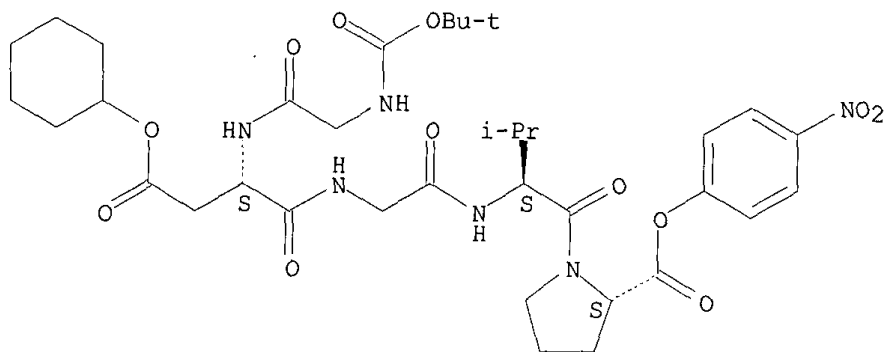
Absolute stereochemistry.



RN 170742-60-6 HCAPLUS

CN L-Proline, 1-[N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-.alpha.-aspartyl]glycyl]-L-valyl]-, 4-cyclohexyl 2-(4-nitrophenyl) ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 12

L23 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:624577 HCAPLUS

DOCUMENT NUMBER: 123:286618

TITLE: Effect of hydrophobic amino acid residue on the stabilization of amphipathic .beta.-structure

AUTHOR(S): Yamamoto, Yoichi; Ono, Shin; Sakai, Yukiko; Yoshimura, Toshiaki; Shimasaki, Choichiro; Tsukurimichi, Eiichi
CORPORATE SOURCE: Faculty Engineering, Toyama University, Toyama, 930, JapanSOURCE: Pept. Chem. (1995), Volume Date 1994, 32nd, 473-6
CODEN: PECHDP; ISSN: 0388-3698

DOCUMENT TYPE: Journal

LANGUAGE: English

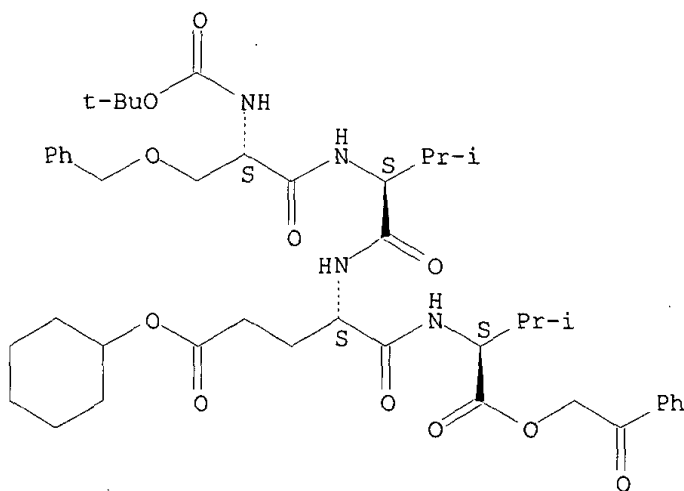
AB Linear octapeptides composed of alternating hydrophilic and hydrophobic amino acid residues were prepd. and found to assume amphipathic .beta.-structure in aq. soln. in peptide concn.- and pH-dependent manner. Hydrophobic amino acid residues having side-chains branched at .beta.-carbon were suggested to be favorable for stabilization of amphipathic .beta.-structure as predicted for globular proteins.

IT 169753-24-6P 169753-26-8P 169753-27-9P
169753-28-0P 169753-41-7P 169753-42-8P
169753-43-9P 169753-44-0P 169753-45-1P
169753-46-2P 169753-47-3P 169753-48-4P
169753-49-5P 169753-50-8P 169753-51-9P
169753-52-0P 169753-54-2P 169753-56-4P
169753-58-6P 169753-60-0P 169753-61-1P
169753-62-2P 169753-63-3P 169753-64-4PRL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(effect of **hydrophobic** amino acid residue on stabilization of amphipathic beta-structure)

RN 169753-24-6 HCAPLUS

CN L-Valine, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-valyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



12, 14

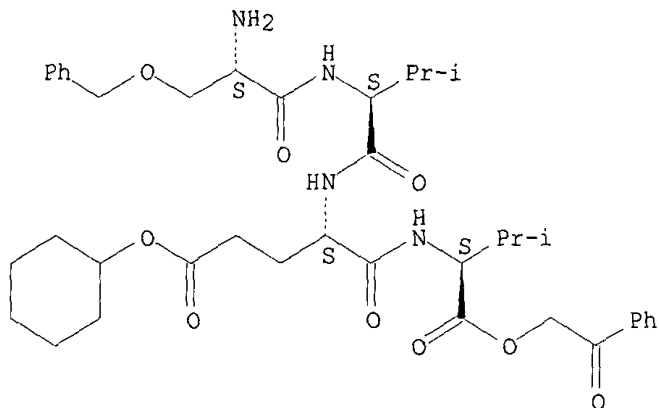
w/ ring = E

RN 169753-26-8 HCAPLUS
 CN L-Valine, N-[N-[N-[O-(phenylmethyl)-L-seryl]-L-valyl]-L-.alpha.-glutamyl]-
 , 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester, mono(trifluoroacetate) (9CI)
 (CA INDEX NAME)

CM 1

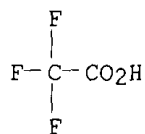
CRN 169753-25-7
 CMF C39 H54 N4 O9
 CDES 5:ALL,L

Absolute stereochemistry.



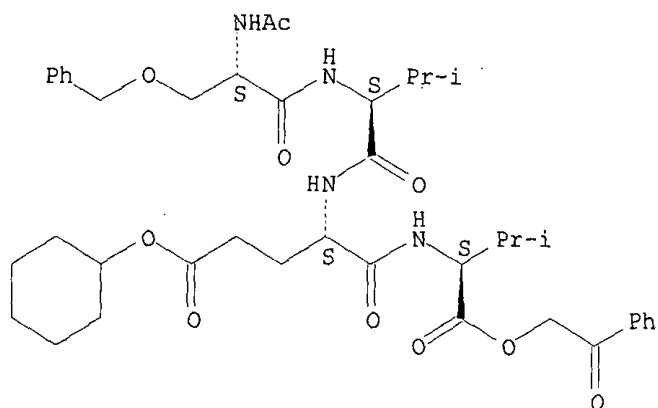
CM 2

CRN 76-05-1
 CMF C2 H F3 O2



RN 169753-27-9 HCAPLUS
 CN L-Valine, N-[N-[N-[N-acetyl-O-(phenylmethyl)-L-seryl]-L-valyl]-L-.alpha.-
 glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX
 NAME)

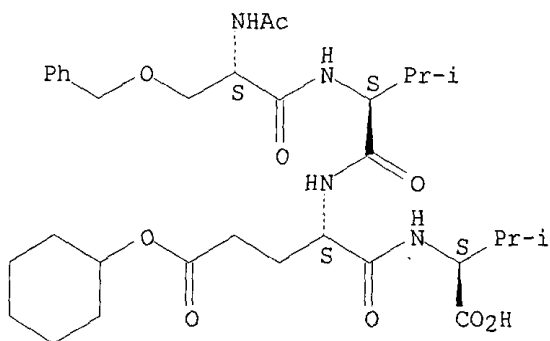
Absolute stereochemistry.



RN 169753-28-0 HCAPLUS

CN L-Valine, N-[N-[N-[N-acetyl-O-(phenylmethyl)-L-seryl]-L-valyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl ester (9CI) (CA INDEX NAME)

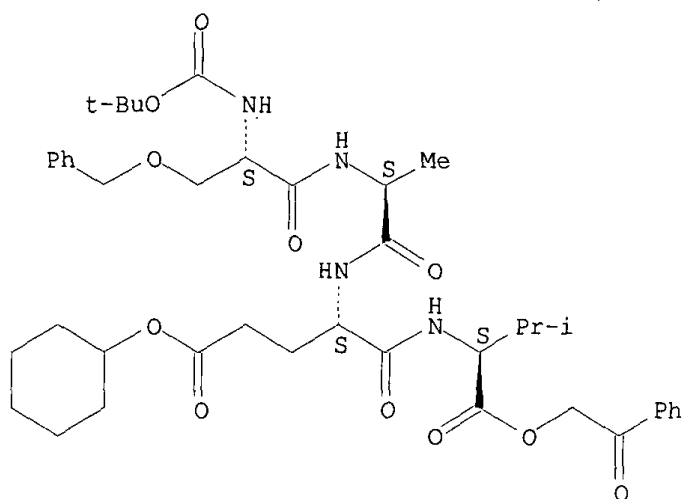
Absolute stereochemistry.



RN 169753-41-7 HCAPLUS

CN L-Valine, N-[N-[N-[N-(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-alanyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX NAME)

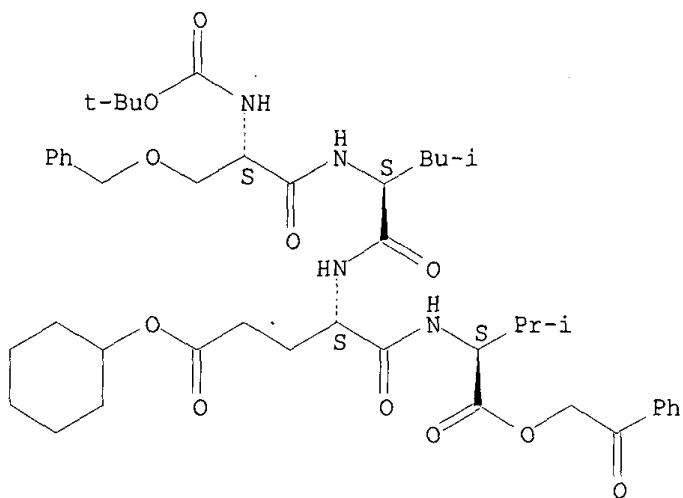
Absolute stereochemistry.



RN 169753-42-8 HCAPLUS

CN L-Valine, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-leucyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX NAME)

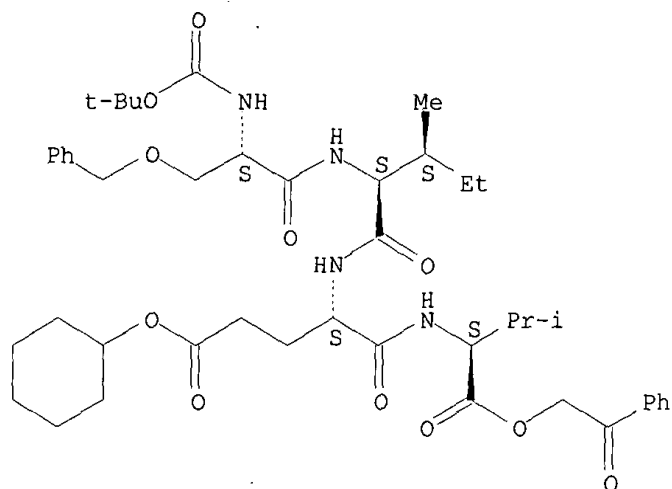
Absolute stereochemistry.



RN 169753-43-9 HCAPLUS

CN L-Valine, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-isoleucyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX NAME)

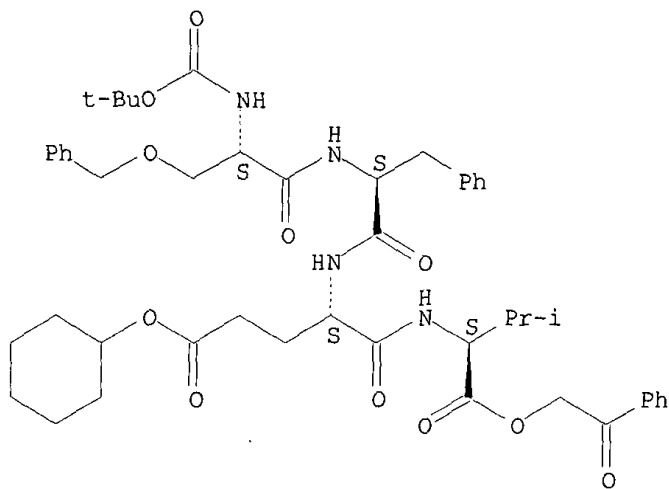
Absolute stereochemistry.



RN 169753-44-0 HCAPLUS

CN L-Valine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-phenylalanyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA INDEX NAME)

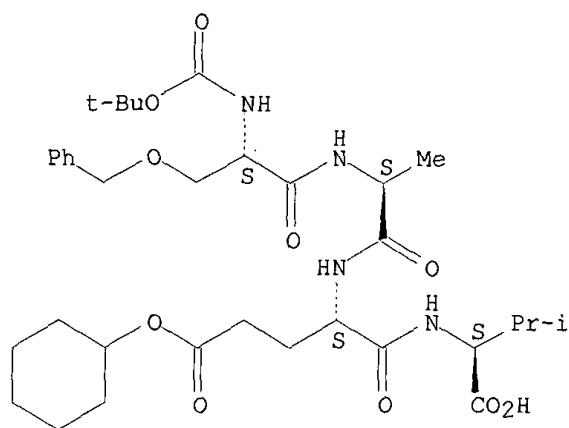
Absolute stereochemistry.



RN 169753-45-1 HCAPLUS

CN L-Valine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-alanyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl ester (9CI) (CA INDEX NAME)

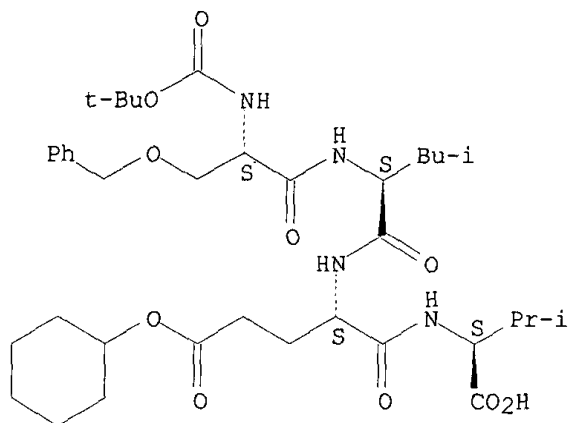
Absolute stereochemistry.



RN 169753-46-2 HCAPLUS

CN L-Valine, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-leucyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl ester (9CI) (CA INDEX NAME)

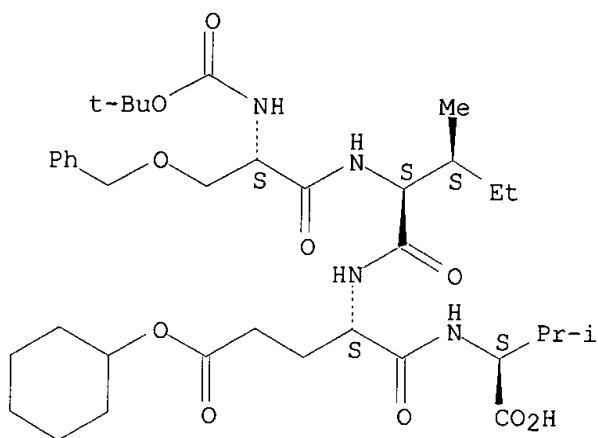
Absolute stereochemistry.



RN 169753-47-3 HCAPLUS

CN L-Valine, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-isoleucyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl ester (9CI) (CA INDEX NAME)

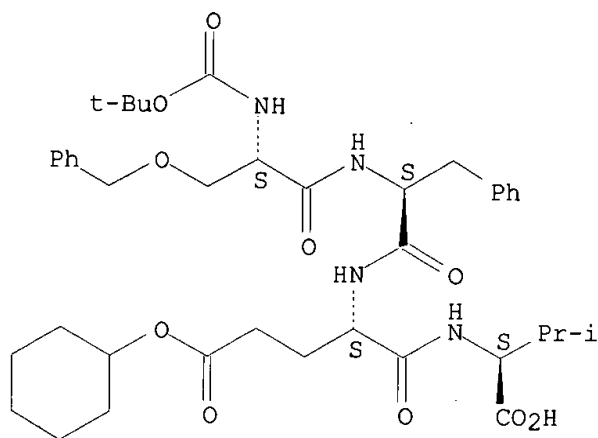
Absolute stereochemistry.



RN 169753-48-4 HCAPLUS

CN L-Valine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-phenylalanyl]-L-.alpha.-glutamyl]-, 5-cyclohexyl ester (9CI) (CA INDEX NAME)

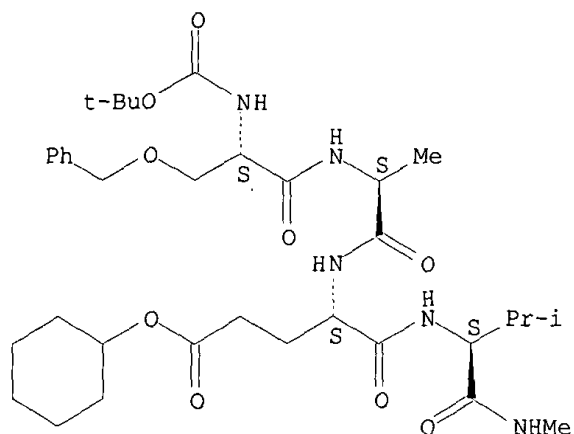
Absolute stereochemistry.



RN 169753-49-5 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl-L-alanyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)

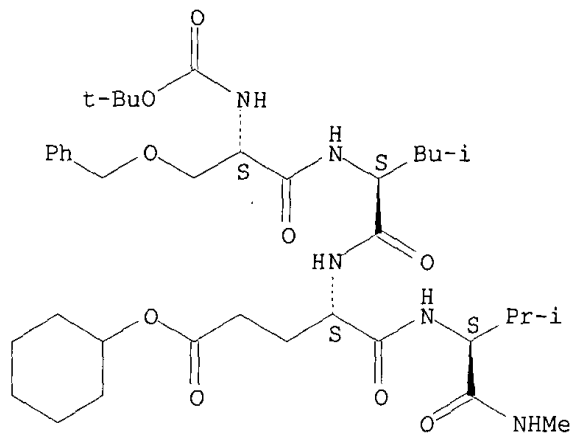
Absolute stereochemistry.



RN 169753-50-8 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl-L-leucyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)

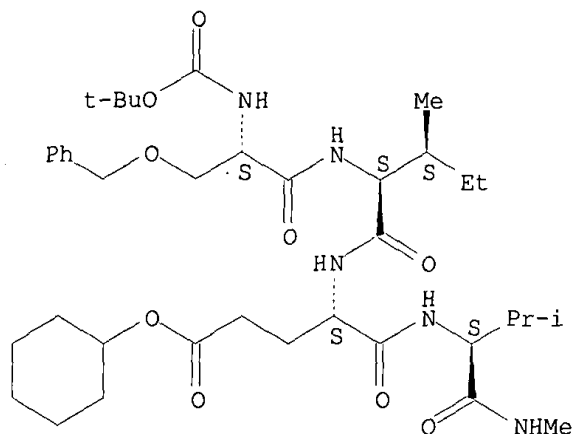
Absolute stereochemistry.



RN 169753-51-9 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl-L-isoleucyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)

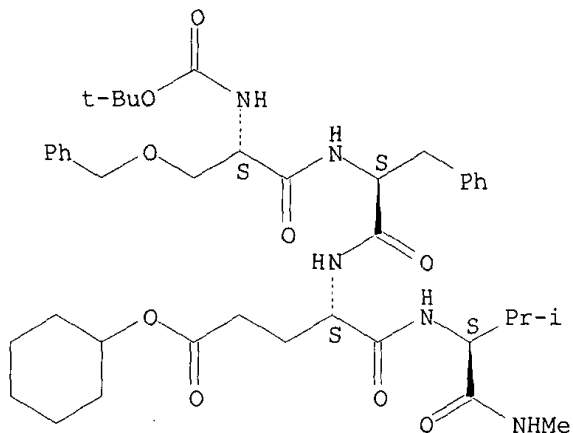
Absolute stereochemistry.



RN 169753-52-0 HCAPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169753-54-2 HCAPLUS

CN L-Valinamide, O-(phenylmethyl)-L-seryl-L-alanyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

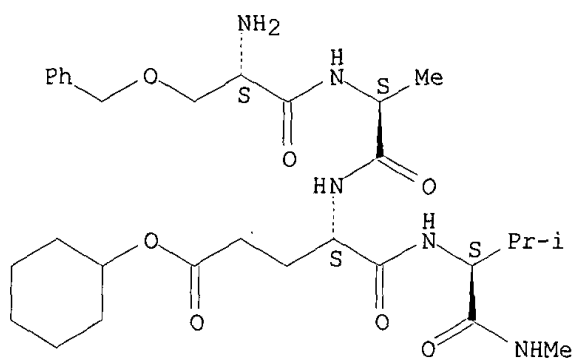
CM 1

CRN 169753-53-1

CMF C30 H47 N5 O7

CDES 5:ALL,L

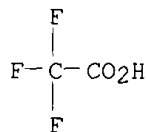
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 169753-56-4 HCAPLUS

CN L-Valinamide, O-(phenylmethyl)-L-seryl-L-leucyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

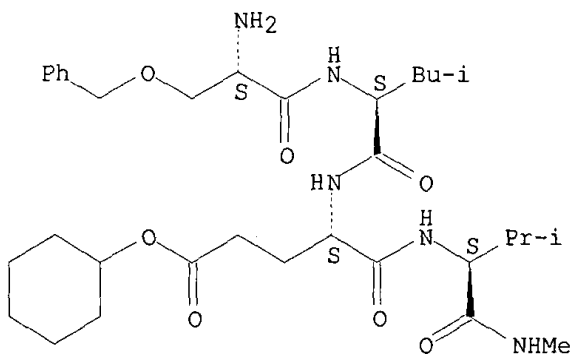
CM 1

CRN 169753-55-3

CMF C33 H53 N5 O7

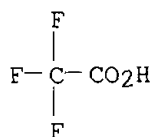
CDES 5:ALL,L

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

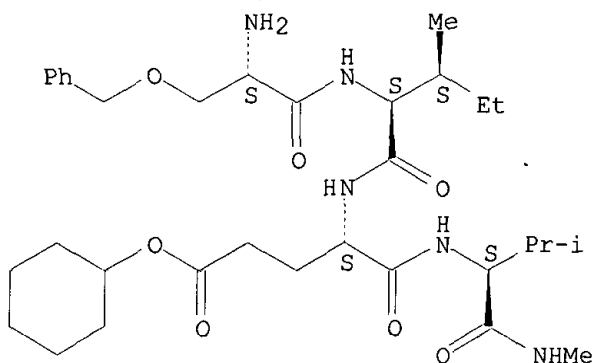


RN 169753-58-6 HCAPLUS
CN L-Valinamide, O-(phenylmethyl)-L-seryl-L-isoleucyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

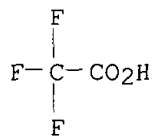
CRN 169753-57-5
CMF C33 H53 N5 O7
CDES 5:ALL,L

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



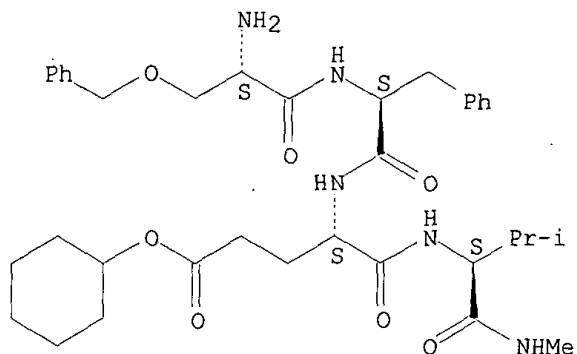
RN 169753-60-0 HCAPLUS
CN L-Valinamide, O-(phenylmethyl)-L-seryl-L-phenylalanyl-L-.alpha.-glutamyl-N-methyl-, cyclohexyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169753-59-7
CMF C36 H51 N5 O7

CDES 5:ALL,L

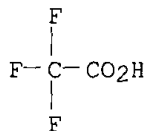
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

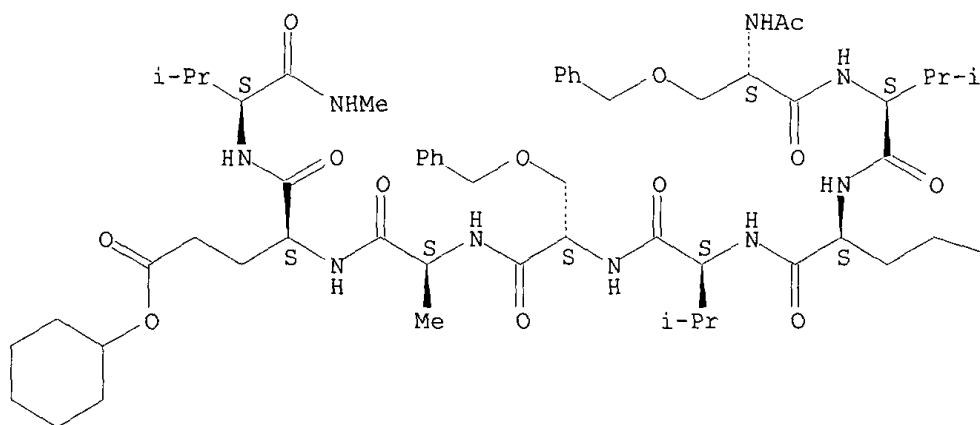


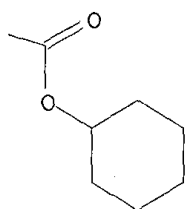
RN 169753-61-1 HCAPLUS

CN L-Valinamide, N-acetyl-O-(phenylmethyl)-L-seryl-L-valyl-L-.alpha.-glutamyl-L-valyl-O-(phenylmethyl)-L-seryl-L-alanyl-L-.alpha.-glutamyl-N-methyl-, dicyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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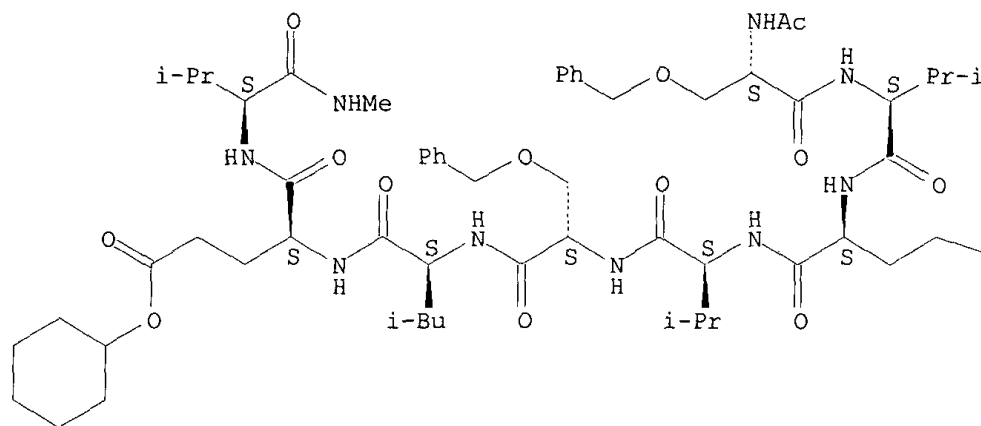




RN 169753-62-2 HCAPLUS
 CN L-Valinamide, N-acetyl-O-(phenylmethyl)-L-seryl-L-valyl-L-.alpha.-glutamyl-L-valyl-O-(phenylmethyl)-L-seryl-L-leucyl-L-.alpha.-glutamyl-N-methyl-, dicyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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CANELLA 09/544,644

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L23 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:88461 HCAPLUS

DOCUMENT NUMBER: 114:88461

TITLE: Sequential polydepsipeptides as biodegradable carriers for drug delivery systems

AUTHOR(S): Yoshida, Masaru; Asano, Masaharu; Kumakura, Minoru; Katakai, Ryoichi; Mashimo, Tooru; Yuasa, Hisako; Imai, Kyoichi; Yamanaka, Hidetoshi

CORPORATE SOURCE: Takasaki Radiat. Chem. Res. Establ., Japan At. Energy Res. Inst., Takasaki, 370-12, Japan

SOURCE: J. Biomed. Mater. Res. (1990), 24(9), 1173-84

CODEN: JBMRBG; ISSN: 0021-9304

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sequential polydepsipeptides contg. both peptide and ester bonds, poly[(L-alanyl)n-.gamma.-Et L-glutamyl-L-lactyl] (n = 0, 1, 2, and 3) (poly[(Ala)n-Glu(OEt)-Lac]), were prepd. for application as biodegradable carriers for drug delivery systems. The in vivo degrdn. of these polymers was evaluated by s.c. implantation in the backs of male rats, and was strongly influenced by the no. (n) of Ala units in poly[(Ala)n-Glu(OEt)-Lac]. The resulting poly(Ala-Ala-Glu(OEt)-Lac) gave the highest degradability, in which 100% degrdn. was obsd. 24 wk from the start of implantation. A luteinizing-hormone-releasing hormone agonist des-Gly10-[D-Leu6]-LH-RH ethylamide (LH-RH agonist), was incorporated into a sequential poly(Ala-Ala-Glu(OEt)-Lac) carrier by the melt-pressing technique, which gave fine cylindrical polymer formulations with different structures of drug dispersion, e.g., blend-type and sandwich-type formulations. The rate of in vivo release of LH-RH agonist from a blend-type formulation showed a linear decrease with time until its release was finished after 6 wk' implantation. In contrast, in a sandwich-type formulation, the in vivo release rate was apparently maintained const. over a period of 16 wk (24 mg/day).

IT 130927-96-7P 130943-90-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as biodegradable **drug delivery** system)

RN 130927-96-7 HCAPLUS

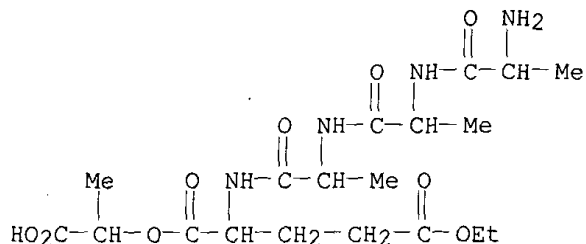
CN L-Glutamic acid, N-[N-(N-L-alanyl-L-alanyl)-L-alanyl]-, 1-(1-carboxyethyl) 5-ethyl ester, (S)-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 130927-95-6

CMF C19 H32 N4 O9

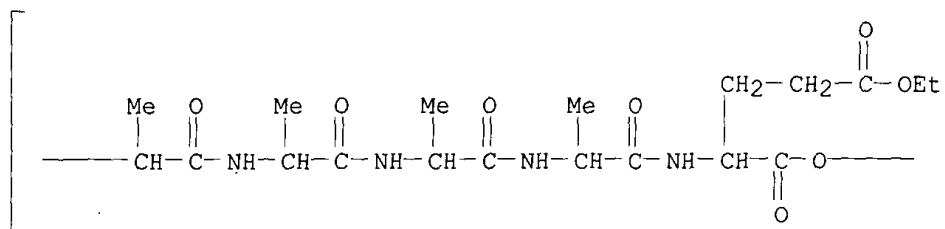
CDES *



RN 130943-90-7 HCAPLUS

CN Poly[oxy[2-(3-ethoxy-3-oxopropyl)-1-oxo-1,2-ethanediyl]imino(2-methyl-1-oxo-1,2-ethanediyl)imino(2-methyl-1-oxo-1,2-ethanediyl)imino(2-methyl-1-oxo-1,2-ethanediyl)imino(2-methyl-1-oxo-1,2-ethanediyl)], stereoisomer (9CI) (CA INDEX NAME)

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$$\left[\begin{array}{c} \text{---} \end{array} \right]_n$$

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L23 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:34506 HCAPLUS

DOCUMENT NUMBER: 108:34506

TITLE: Membrane anchor conjugates with active agents, their preparation and uses

PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.

SOURCE: Ger. Offen., 34 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| DE 3546150 | A1 | 19870122 | DE 1985-3546150 | 19851227 |
| FI 8602631 | A | 19861225 | FI 1986-2631 | 19860619 |
| FI 94419 | B | 19950531 | | |
| FI 94419 | C | 19950911 | | |
| EP 210412 | A2 | 19870204 | EP 1986-108324 | 19860619 |
| EP 210412 | A3 | 19900207 | | |
| EP 210412 | B1 | 19951213 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| AT 131491 | E | 19951215 | AT 1986-108324 | 19860619 |
| DK 8602940 | A | 19861225 | DK 1986-2940 | 19860623 |
| DK 172399 | B1 | 19980518 | | |
| NO 8602511 | A | 19861229 | NO 1986-2511 | 19860623 |
| NO 174207 | B | 19931220 | | |
| NO 174207 | C | 19940330 | | |
| AU 8658943 | A1 | 19870108 | AU 1986-58943 | 19860623 |
| AU 611385 | B2 | 19910613 | | |
| ZA 8604657 | A | 19870225 | ZA 1986-4657 | 19860623 |
| JP 62063600 | A2 | 19870320 | JP 1986-145031 | 19860623 |
| ES 556417 | A1 | 19880216 | ES 1986-556417 | 19860623 |
| SU 1823876 | A3 | 19930623 | SU 1986-4027766 | 19860623 |
| NO 9200356 | A | 19861229 | NO 1992-356 | 19920127 |
| US 6024964 | A | 20000215 | US 1995-466695 | 19950606 |
| US 6074650 | A | 20000613 | US 1995-465709 | 19950606 |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|----------|
| DE 1985-3522512 | A1 | 19850624 |
| DE 1985-3546150 | A | 19851227 |
| US 1986-876479 | B1 | 19860620 |
| NO 1986-2511 | A1 | 19860623 |
| DE 1988-3813821 | A | 19880422 |
| US 1988-229770 | B1 | 19880801 |
| US 1989-340833 | B2 | 19890420 |
| US 1989-427914 | B1 | 19891024 |
| DE 1989-3937412 | A | 19891110 |
| US 1990-588794 | B2 | 19900827 |
| US 1990-610222 | B1 | 19901108 |
| US 1992-966603 | B2 | 19921026 |
| US 1993-84091 | B1 | 19930630 |
| US 1995-387624 | B3 | 19950213 |

AB Active agents (antigens, antibiotics, hormones, enzymes, labels, etc.) are conjugated to compds. which can be inserted into cell membranes. The conjugates are useful e.g. to promote cell fusion, to provide cells with fluorescent or spin labels, etc. The extracytoplasmic region of the EGF receptor encompassing residues 516-529 was constructed by the Merrifield

resin method, coupled to fluorenylmethoxycarbonyl(tert-butyl)serine and S-[2,3-bis(palmitoyloxy)propyl]-N-palmitoylcysteinyserine(Pam3Cys-Ser) (the N-terminus of the outer membrane lipoprotein of Escherichia coli) as adjuvant, cleaved from the resin, and administered once i.p. to mice. A high titer of antibodies to the EGF receptor peptide was detected within 2 wk.

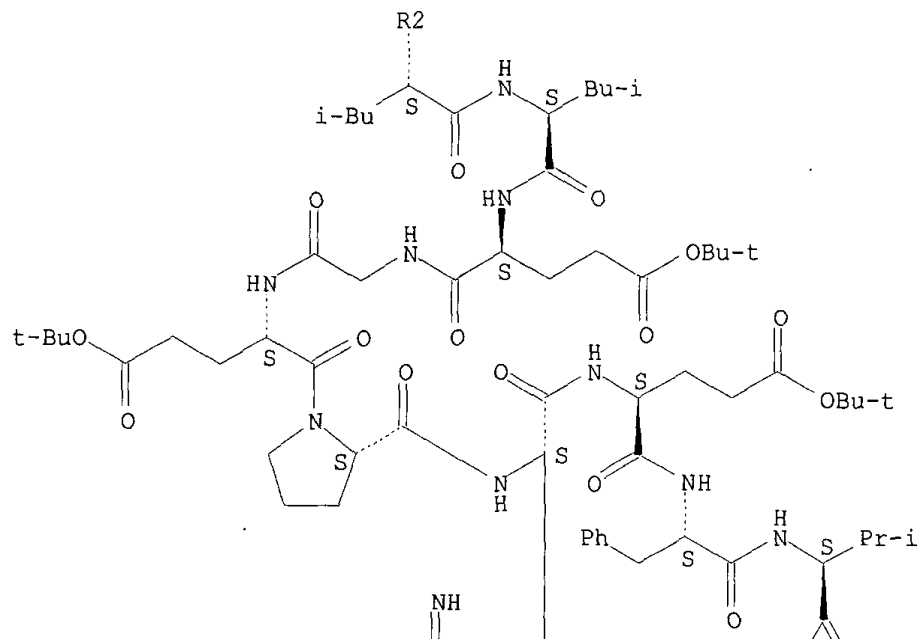
IT **112208-19-2DP**, alkoxybenzyl esters, reaction products with styrene-divinylbenzene copolymer
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, in prepn. of EGF peptide-membrane anchor **conjugates**)

RN 112208-19-2 HCAPLUS

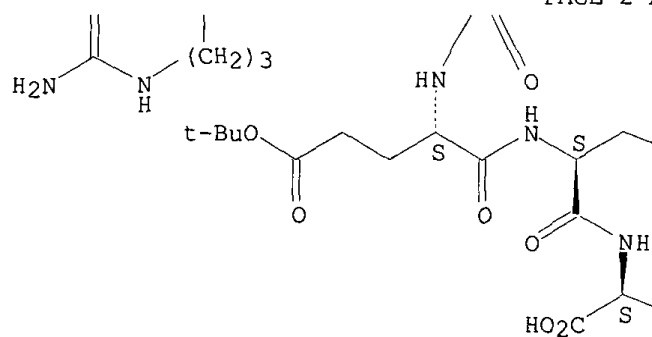
CN L-Serine, S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-N-(1-oxohexadecyl)-L-cysteinyl-O-(1,1-dimethylethyl)-L-seryl-L-asparaginyl-L-leucyl-L-leucyl-L-.alpha.-glutamylglycyl-L-.alpha.-glutamyl-L-prolyl-L-arginyl-L-.alpha.-glutamyl-L-phenylalanyl-L-valyl-L-.alpha.-glutamyl-L-asparaginyl-O-(1,1-dimethylethyl)-, 6,8,11,14-tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

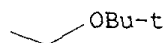
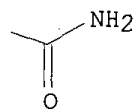
PAGE 1-A



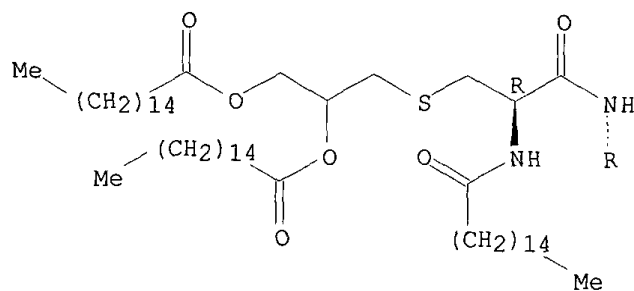
PAGE 2-A

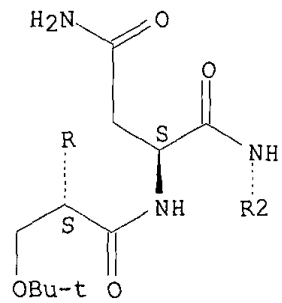


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PAGE 3-A





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L24 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:816796 HCAPLUS
 DOCUMENT NUMBER: 135:359144
 TITLE: Sulfonated [8,9]benzophenoxazine dyes and the use of
 their labelled conjugates
 INVENTOR(S): Yan, Xiongwei; Yuan, Pau Miao
 PATENT ASSIGNEE(S): Applera Corporation, USA
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-----------|---------------------------|----------|
| WO 2001083621 | A2 | 200111108 | WO 2001-US14110 | 20010501 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-564417 A 20000502 | |

OTHER SOURCE(S): MARPAT 135:359144

AB Fluorescent, sulfonated 3,7-diamino-[8,9]benzophenoxazine dyes are provided that are esp. useful for labeling biopolymers and other substrates. The dye-labeled conjugates can be used in a variety of contexts, including cell surface assays employing intact, live cells and in nucleic acid detection methods. The new dyes are water sol. and can be conjugated to a variety of substrates, such as polynucleotides, nucleosides, nucleotides, peptides, proteins, antibodies, carbohydrates, ligands, particles and surfaces.

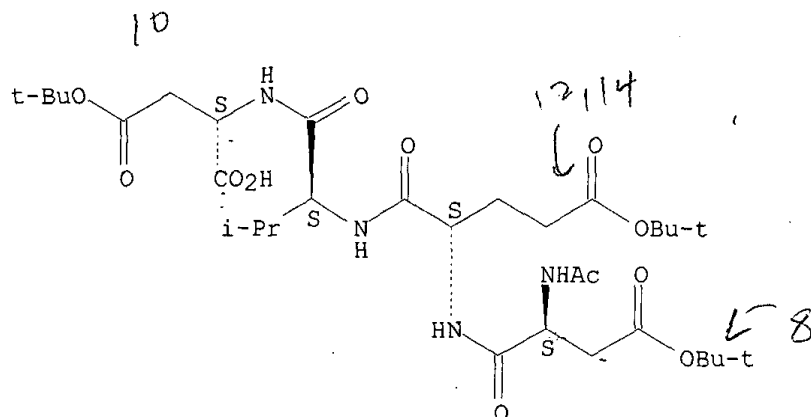
IT 223539-69-3P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of sulfonated [8,9]benzophenoxazine dyes and their use as labeled **conjugates**)

RN 223539-69-3 HCAPLUS

CN L-Aspartic acid, N-acetyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-valyl-, 1,2,44-tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:798301 HCAPLUS

DOCUMENT NUMBER: 135:348868

TITLE: RGD (Arg-Gly-Asp) coupled to (neuro)peptides

INVENTOR(S): De Jong, Marion; Krenning, Eric Paul; Van Hagen, Petrus Martinus

PATENT ASSIGNEE(S): Mallinckrodt, Inc., USA

SOURCE: PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001081426 | A2 | 20011101 | WO 2001-EP4764 | 20010426 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: EP 2000-201499 A 20000426

AB The invention relates to compds. having a binding affinity for both the .alpha.v.beta.3 receptor and a (neuro)peptide receptor, in particular the somatostatin receptor, which compd. comprises a first peptide part comprising at least once the amino acid sequence Arg-Gly-Asp, and a second peptide part coupled thereto, optionally via a linker, which second peptide part is a (neuro)peptide. The peptides may be radiolabeled for autoradiog. expts.

IT **371161-34-1D, resin conjugates 371161-39-6D, resin conjugates**

RL: RCT (Reactant); RACT (Reactant or reagent)

(RGD (Arg-Gly-Asp) coupled to (neuro)peptides for radiolabeling)

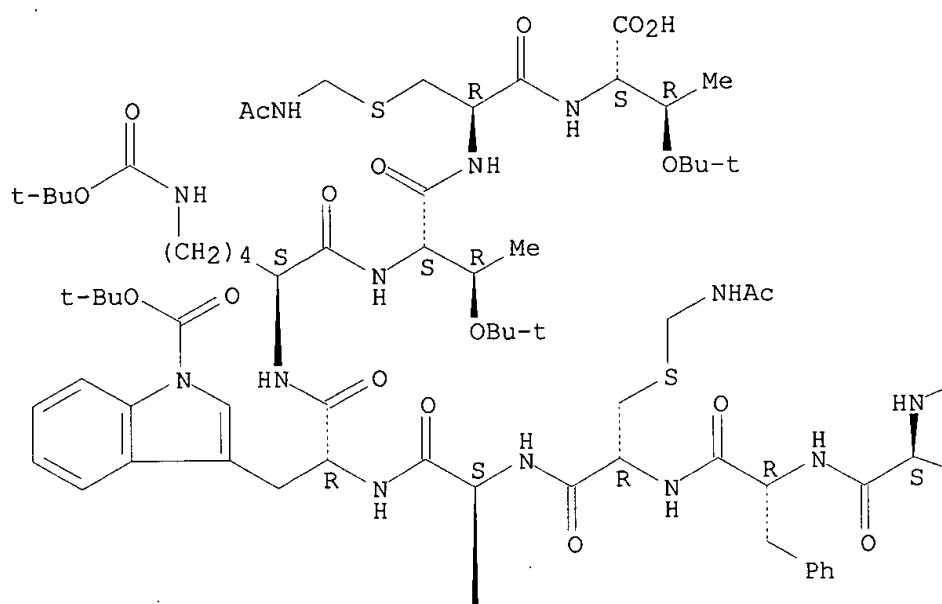
RN 371161-34-1 HCAPLUS

CN L-Threonine, N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-D-tyrosyl-L-.alpha.-aspartyl-N6-[(4-methylphenyl)diphenylmethyl]-L-lysyl-D-phenylalanyl-S-

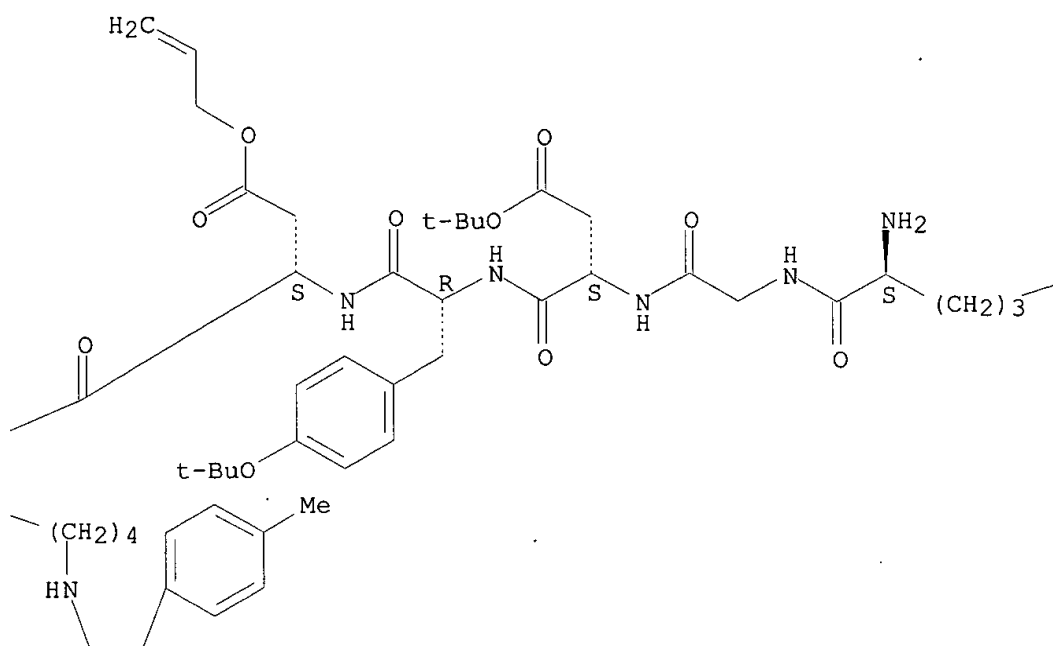
[(acetylamino)methyl]-L-cysteinyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-D-tryptophyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-O-(1,1-dimethylethyl)-L-threonyl-S-[(acetylamino)methyl]-L-cysteinyl-O-(1,1-dimethylethyl)-, 3-(1,1-dimethylethyl) 5-(2-propenyl) ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

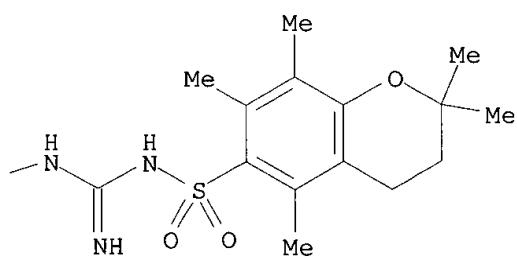
PAGE 1-A



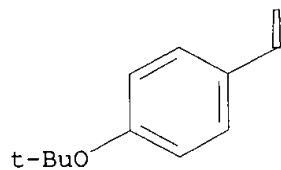
PAGE 1-B

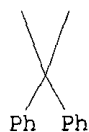


PAGE 1-C



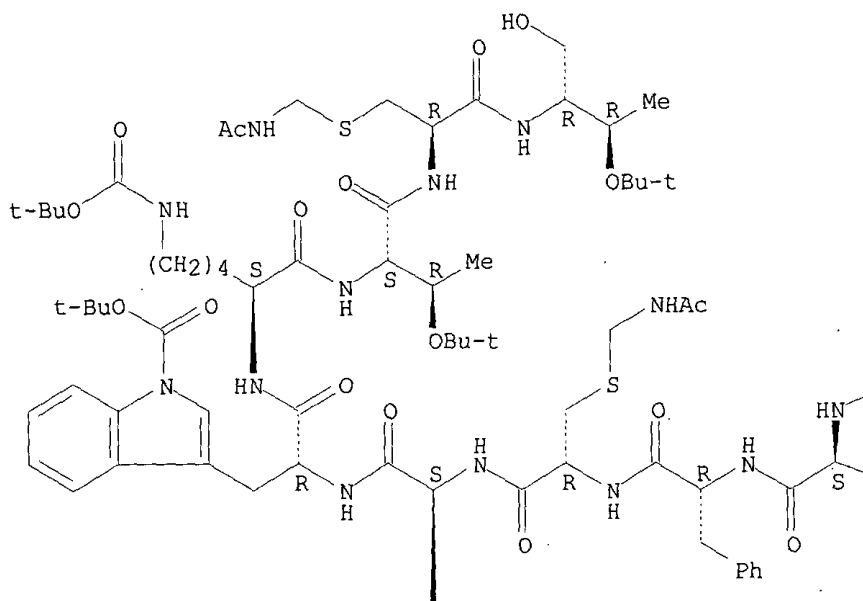
PAGE 2-A



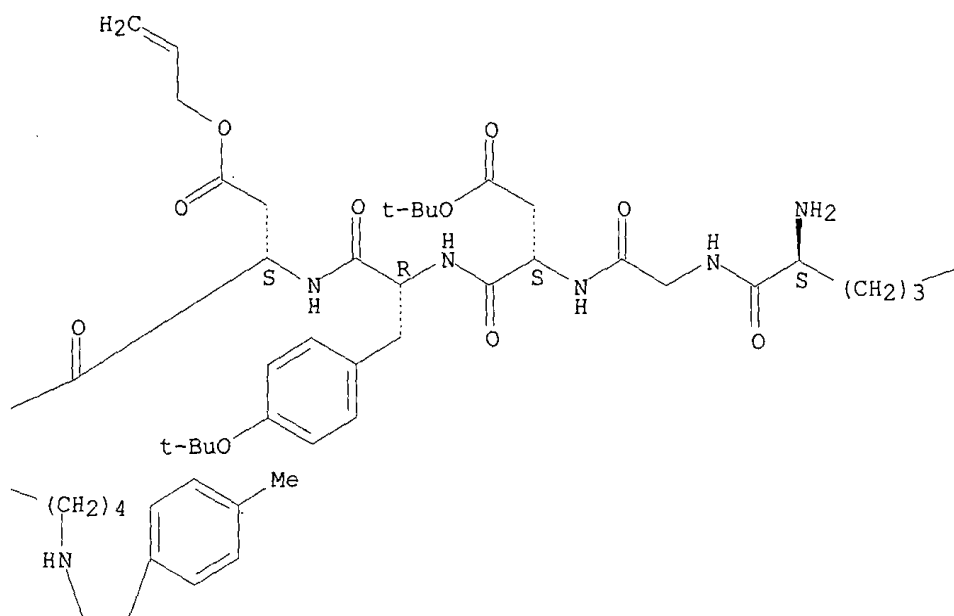


RN 371161-39-6. HCAPLUS
 CN L-Cysteinamide, N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-D-tyrosyl-L-.alpha.-aspartyl-N6-[(4-methylphenyl)diphenylmethyl]-L-lysyl-D-phenylalanyl-S-[(acetylamino)methyl]-L-cysteinyl-O-(1,1-dimethylethyl)-L-tyrosyl-1-[(1,1-dimethylethoxy)carbonyl]-D-tryptophyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-O-(1,1-dimethylethyl)-L-threonyl-S-[(acetylamino)methyl]-N-[(1R,2R)-2-(1,1-dimethylethoxy)-1-(hydroxymethyl)propyl]-, 3-(1,1-dimethylethyl)5-(2-propenyl) ester (9CI) (CA INDEX NAME)

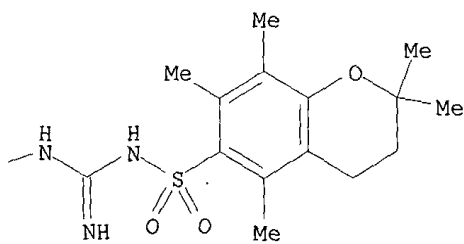
Absolute stereochemistry.



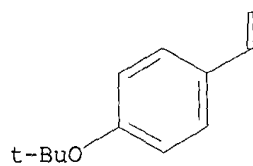
PAGE 1-B



PAGE 1-C



PAGE 2-A





L24 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:743883 HCAPLUS

DOCUMENT NUMBER: 136:135007

TITLE: Highly efficient synthesis of peptide-oligonucleotide conjugates: chemoselective oxime and thiazolidine formation

AUTHOR(S): Forget, Damien; Boturnyn, Didier; Defrancq, Eric; Lhomme, Jean; Dumy, Pascal

CORPORATE SOURCE: LEDSS, UMR CNRS 5616, Universite Joseph Fourier, Grenoble, 38041, Fr.

SOURCE: Chemistry--A European Journal (2001), 7(18), 3976-3984
CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A convergent strategy for the synthesis of peptide-oligonucleotide conjugates (POC) is presented. Chemoselective ligation of peptide to oligonucleotide was accomplished by oxime and thiazolidine formation. Oxime conjugation was performed by treating an oxyamine-contg. peptide with an aldehyde-contg. oligonucleotide or vice versa. Ligation by thiazolidine formation was achieved by coupling a peptide, acylated with a cysteine residue, to an oligonucleotide that was derivatised by an aldehyde function. For both approaches, the conjugates were obtained in good yield without the need for a protection strategy and under mild aq. conditions. Moreover, the oxime ligation proved useful for directly conjugating duplex oligonucleotides. Combined with mol. biol. tools, this methodol. opens up new prospects for post-functionalization of high-mol.-wt. DNA structures.

IT 343312-38-9 388633-60-1D, resin-bound

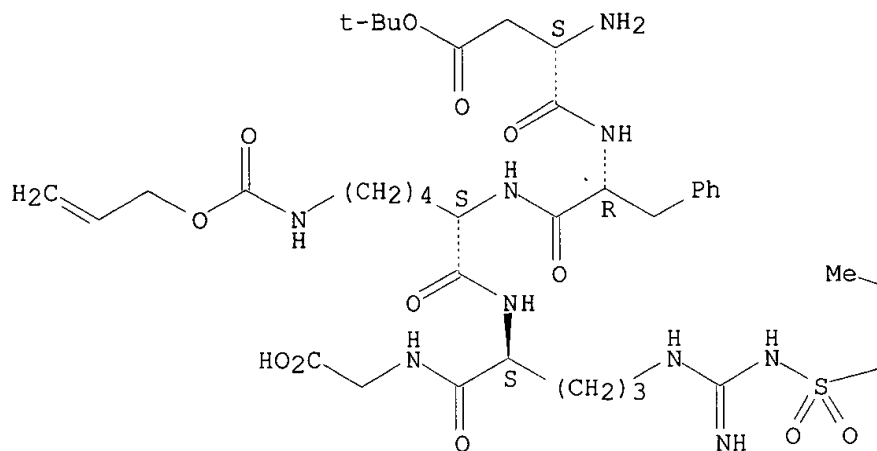
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptide-oligonucleotide **conjugates** via oxime and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)

RN 343312-38-9 HCAPLUS

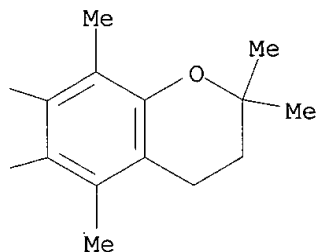
CN Glycine, L-.alpha.-aspartyl-D-phenylalanyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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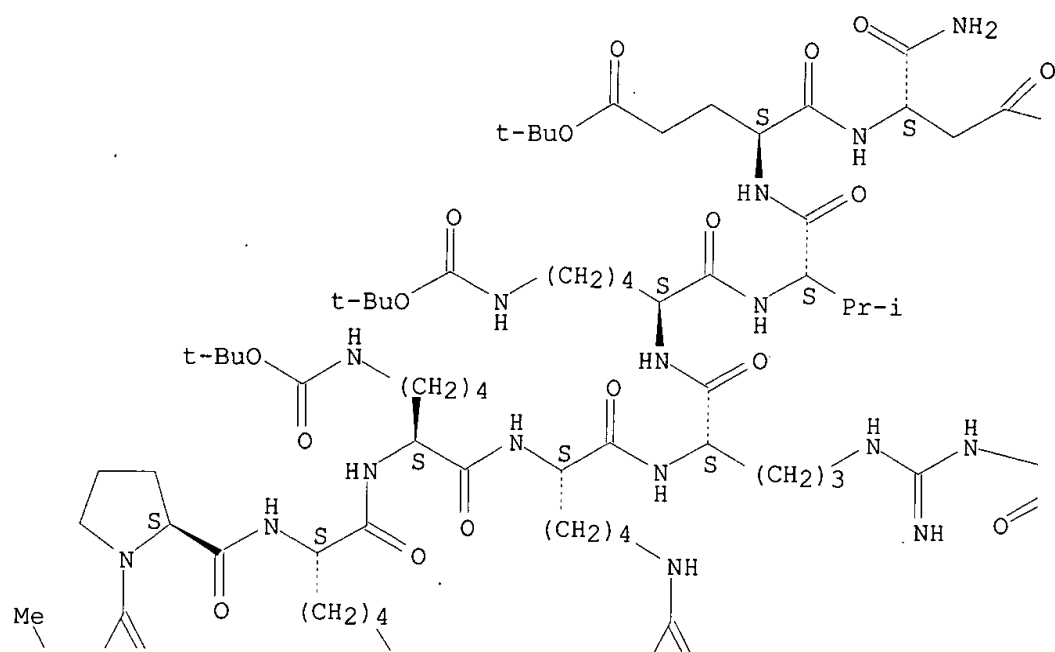


RN 388633-60-1 HCAPLUS

CN L-.alpha.-Asparagine, L-alanyl-L-prolyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-valyl-L-.alpha.-glutamyl-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

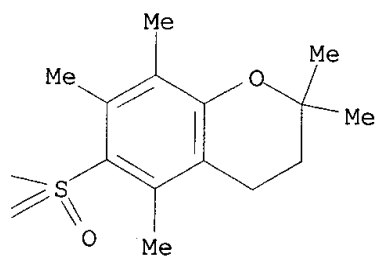
Absolute stereochemistry.

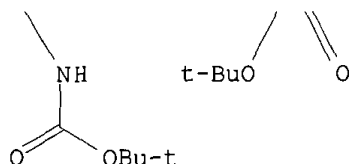
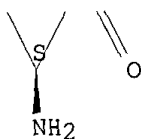
PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:300756 HCAPLUS

DOCUMENT NUMBER: 134:320857

TITLE: Modified peptides and peptidomimetics for use in immunotherapy

INVENTOR(S): Van Staveren, Catherina Joanna; Timmers, Cornelis Marius; Van Galen, Philippus Johannes Marie; Knegtel, Rnaldus Marcellus Alphonsus; Boots, Anna Maria Helena; Miltenburg, Andreas Martinus Maria

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001029081 | A1 | 20010426 | WO 2000-EP10230 | 20001012 |
| W: | AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: EP 1999-203427 A 19991018

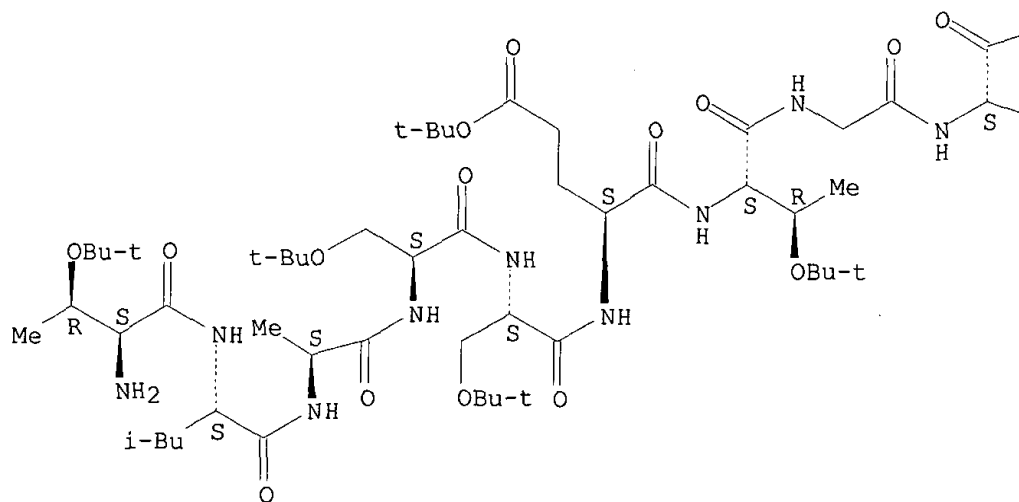
OTHER SOURCE(S): MARPAT 134:320857

AB The invention relates to a modified peptide derived from formula I peptide H-Arg-Ser-Phe-Thr-Leu-Ala-Ser-Ser-Glu-Thr-Gly-Val-Gly-OH (peptide (263-275) of cartilage-derived protein human cartilage gp-39 (HC gp-39)) having general formula (II): Q-A1-A2-A3-A4-A5-A6-A7-A8-A9-A10-A11-A12-A13-Z. In general formula (II), A1 through A13 correspond with the amino acids of formula (I), Q corresponds with H and Z corresponds with OH. The modifications according to the present invention are selected from one or more of the groups a, b or c, consisting of (a) substitution of 1-6, preferably 1-4 amino acids at A1 through A13 with non-natural amino acids or .beta. amino acids; (b) substitution of one or more amide bonds with reduced amide bonds or ethylene isosteres; (c) substitutions at Q and/or Z and, optionally, (d) substitution of natural amino acids up to a total of 6 modifications. The peptides can be used for inducing tolerance induction in patients suffering from autoimmune diseases. The most potent compds. were Ac-Arg-Ser-Phe-Thr-Leu-Ala-Ser-Ser-Glu-Thr-Gly-Val-Gly-OH, Ac-Arg-Ser-Phe-Thr-Leu-Ala-Ser-Ser-Glu-Thr-Gly-Val-.psi.[CH2NH]-Gly-NH2, Ac-Arg-NhSer-Phe-Thr-Leu-Ala-Ser-Ser-Glu-Thr-Gly-Val-Gly-NH2 and Ac-Arg-NhSer-Phe-Thr-Leu-Ala-Ser-Ser-Glu-Thr-Gly-Val-.psi.[CH2NH]-Gly-NH2.

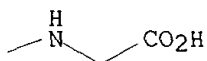
IT **335598-61-3D, conjugates** with PAC-PEG-PS resin
 RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
 (modified peptides and peptidomimetics based on peptide from human
 cartilage glycoprotein 39 for use in immunotherapy)
 RN 335598-61-3 HCAPLUS
 CN Glycine, O-(1,1-dimethylethyl)-L-threonyl-L-leucyl-L-alanyl-O-(1,1-
 dimethylethyl)-L-seryl-O-(1,1-dimethylethyl)-L-seryl-L-.alpha.-glutamyl-O-
 (1,1-dimethylethyl)-L-threonylglycyl-L-valyl-, 6-(1,1-dimethylethyl) ester
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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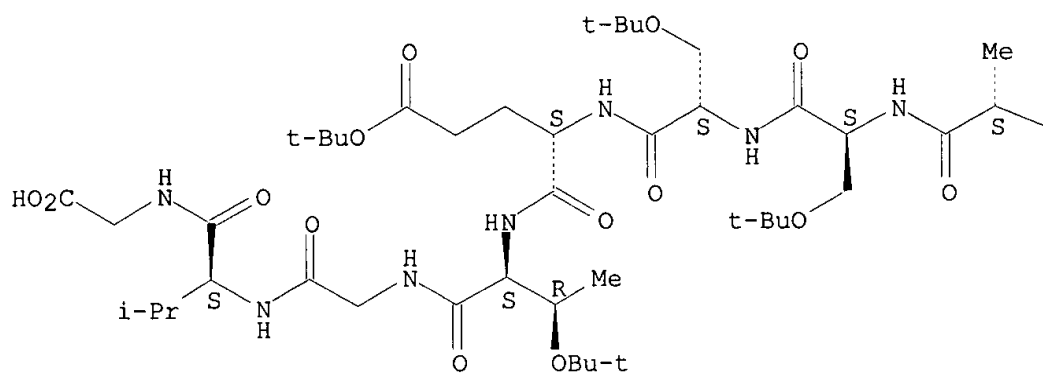


Pr-i

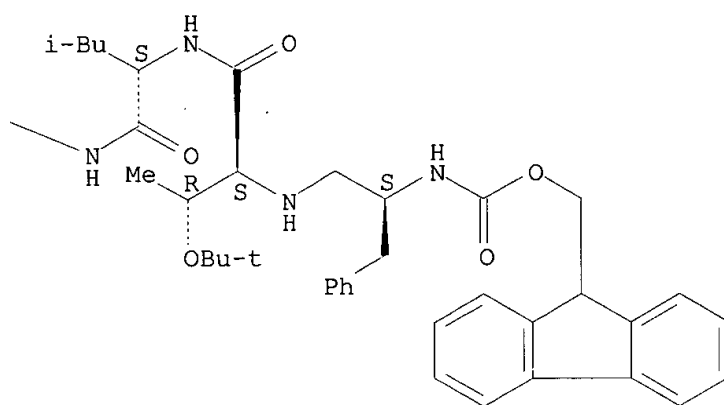
IT **335598-62-4DP, conjugates** with PAL-PEG-PS resin
335598-68-0DP, conjugates with PAL-PEG-PS resin
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (modified peptides and peptidomimetics based on peptide from human
 cartilage glycoprotein 39 for use in immunotherapy)
 RN 335598-62-4 HCAPLUS
 CN Glycine, O-(1,1-dimethylethyl)-N-[(2S)-2-[[[(9H-fluoren-9-
 ylmethoxy)carbonyl]amino]-3-phenylpropyl]-L-threonyl-L-leucyl-L-alanyl-O-
 (1,1-dimethylethyl)-L-seryl-O-(1,1-dimethylethyl)-L-seryl-L-.alpha.-
 glutamyl-O-(1,1-dimethylethyl)-L-threonylglycyl-L-valyl-,
 6-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



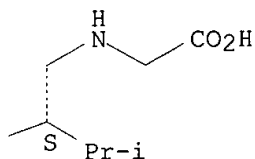
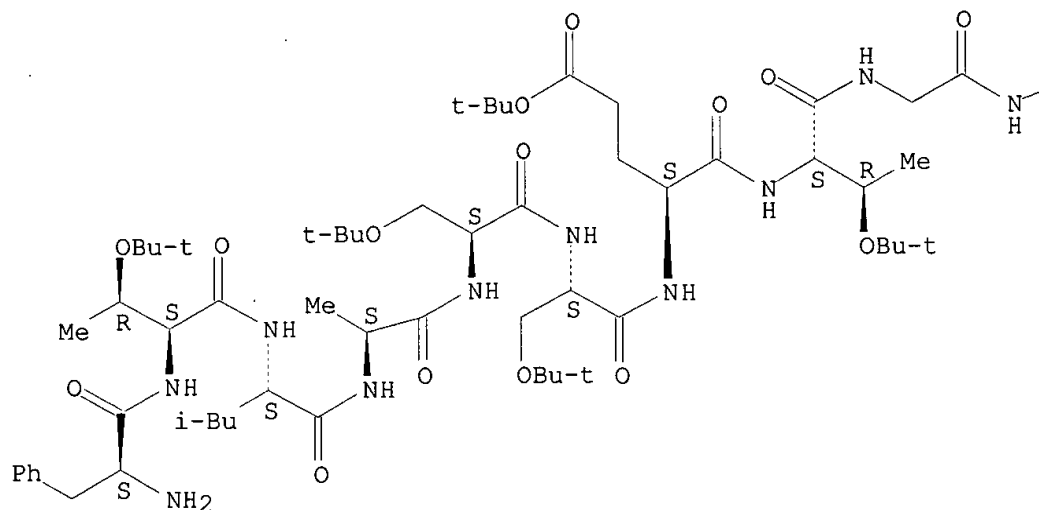
PAGE 1-B



RN 335598-68-0 HCAPLUS

CN Glycine, L-phenylalanyl-O-(1,1-dimethylethyl)-L-threonyl-L-leucyl-L-alanyl-O-(1,1-dimethylethyl)-L-seryl-O-(1,1-dimethylethyl)-L-seryl-L-.alpha.-glutamyl-O-(1,1-dimethylethyl)-L-threonylglycyl-L-valyl-.psi.(CH2-NH)-, 7-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:87230 HCAPLUS

DOCUMENT NUMBER: 134:252642

TITLE: Towards the development of antitumor vaccines: a synthetic conjugate of a tumor-associated MUC1 glycopeptide antigen and a tetanus toxin epitope
 AUTHOR(S): Keil, Stefanie; Claus, Christine; Dippold, Wolfgang; Kunz, Horst

CORPORATE SOURCE: Institut für Organische Chemie der Universität Mainz, Mainz, 55099, Germany

SOURCE: Angewandte Chemie, International Edition (2001), 40(2), 366-369

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In work aimed at synthesis of glycopeptides of the tumor-assocd. mucin NUC1, the authors have prepd. TN-, T-, and sialyl-Tn-antigen glycopeptides from the tandem repeat region of NUC1, in which the tumor-assocd. MUC1 glycopeptide antigen was combines with a T-cell epitope of tetanus toxin using a flexible spacer to prep. a conjugate. The whole construct was

formed from two large portions using a solid-phase condensation technique. For immunol. evaluation, the conjugate was tested on four samples of peripheral blood lymphocytes, with re-stimulation carried out after seven days, leading to prodn. of interferon- γ , proof of antigen-specific reactivity. Anal. showed proliferation of CD3-pos. T-cells, which showed that the conjugate could induce cytotoxic T-cell response.

IT 330846-53-2DP, resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of **conjugate** of a tumor-assocd. MUC1 glycopeptide antigen and a tetanus toxin epitope for use as antitumor vaccine)

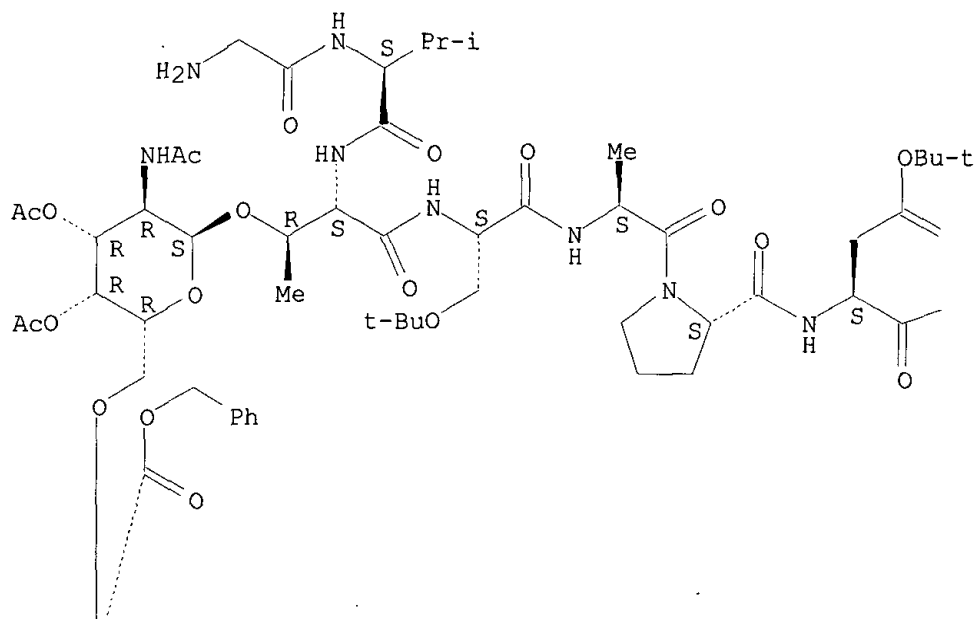
RN 330846-53-2 HCAPLUS

CN .beta.-Alanine, glycyl-L-valyl-O-[3,4-di-O-acetyl-2-(acetylamino)-6-O-[N-acetyl-4,7,8,9-tetra-O-acetyl-1-(phenylmethyl)-.alpha.-neuraminosyl]-2-deoxy-.alpha.-D-galactopyranosyl]-L-threonyl-O-(1,1-dimethylethyl)-L-seryl-L-alanyl-L-prolyl-L-.alpha.-aspartyl-O-(1,1-dimethylethyl)-L-threonyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-prolyl-L-alanyl-L-prolyl-(15E)-17-hydroxy-4,7,10,13-tetraoxaheptadec-15-enoyl-, 7-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

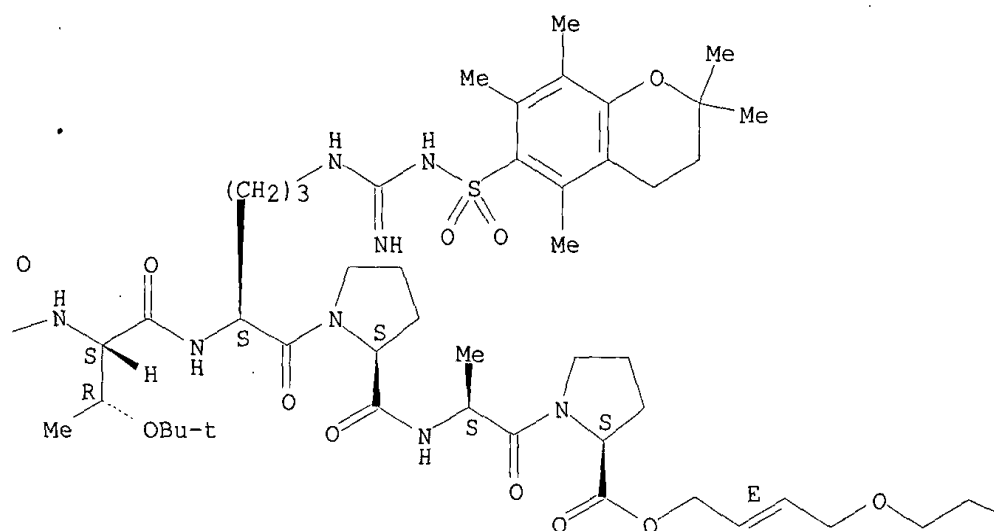
Absolute stereochemistry.

Double bond geometry as shown.

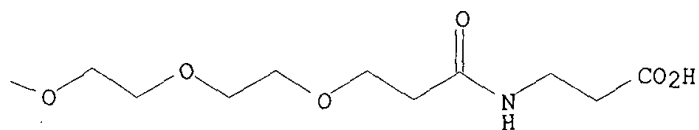
PAGE 1-A

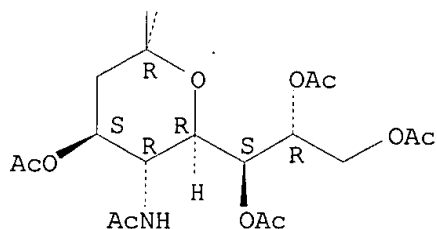


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PAGE 1-C





REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:772489 HCAPLUS

DOCUMENT NUMBER: 133:355232

TITLE: Enzymatically activated polymeric drug conjugates
INVENTOR(S): Pachence, James M.; Belinka, Benjamin A.; Ramani, Thulasi

PATENT ASSIGNEE(S): Veritas Medical Technologies, Inc., USA

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2000064486 | A2 | 20001102 | WO 2000-US11670 | 20000428 |
| WO 2000064486 | A3 | 20010426 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1176985 | A2 | 20020206 | EP 2000-928630 | 20000428 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1999-131404P P 19990428
US 1999-163090P P 19991102
WO 2000-US11670 W 20000428

AB The present invention relates to a polymeric drug conjugate with one or more biol. active agents conjugated via an enzymically cleavable linker to either a regular repeating linear unit comprising a water sol. polymer segment and a multifunctional chem. moiety, or a branched polymer comprising two or more water sol. polymer segments each bound to a common multifunctional chem. moiety, as well as to methods of making such conjugates. The present invention is also directed to pharmaceutical compns. comprising such conjugates and to the use of such conjugates to treat pathol. conditions. A conjugate consisting of Fmoc-doxorubicin-14-O-hemiglutarate deriv. as an active agent, tetrapeptide Val-Gly-Pro-Ala as an enzymically cleaved linker, a multifunctional chem. moiety prepd. from N-fluorenylmethoxycarbonyl-O-tert-butylserine, N-(benzyloxycarbonyl)-

ethane-1,2-diamine, and tetrahydropyranyl ether, and polyethylene glycol 2000 was prepd.

IT 304851-38-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polymeric drug **conjugate** contg. water-sol. polymers and multifunctional chem. moieties and enzymically cleavable linkers and biol. active agents)

RN 304851-38-5 HCAPLUS

CN Glycine, 3-[[3-[[2-[[3,5-dihydroxyphenyl)acetyl]amino]ethyl]amino]-3-oxopropyl]dithio]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-leucyl-2-(5-fluoro-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-, 2,3,4-tris(1,1-dimethylethyl) ester, polymer with .alpha.-[(4-methylphenyl)sulfonyl]-.omega.-[(4-methylphenyl)sulfonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

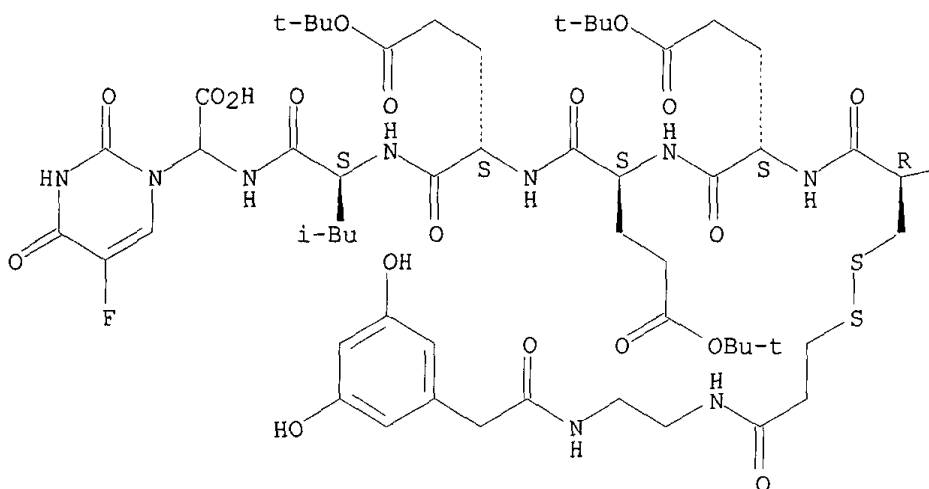
CM 1

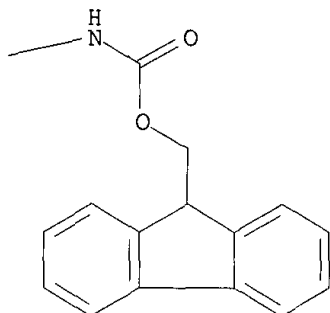
CRN 304851-37-4

CMF C70 H93 F N10 O21 S2

Absolute stereochemistry.

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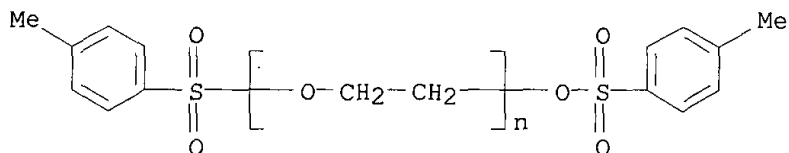


CM 2

CRN 35164-96-6

CMF (C2 H4 O)n C14 H14 O5 S2

CCI PMS



IT 304851-29-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of polymeric drug **conjugate** contg. water-sol.

polymers and multifunctional chem. moieties and enzymically cleavable

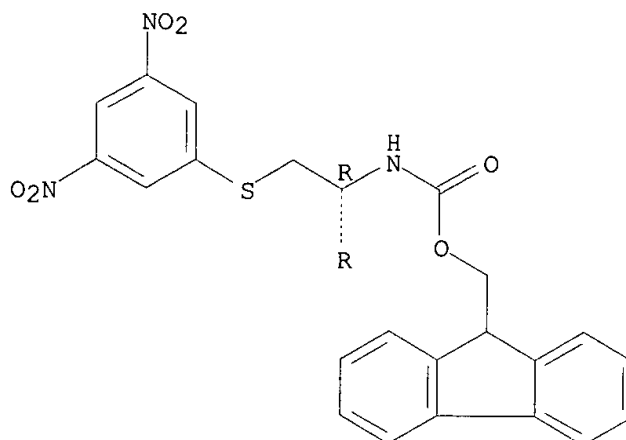
linkers and biol. active agents)

RN 304851-29-4 HCAPLUS

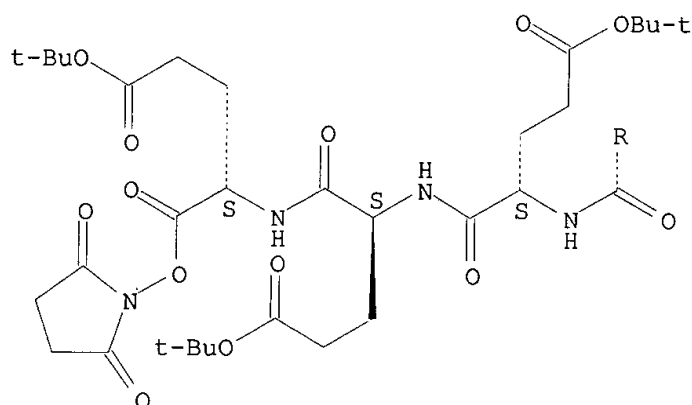
CN 2,5-Pyrrolidinedione, 1-[[S-(3,5-dinitrophenyl)-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-cysteinyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl]oxy]-, tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 304851-30-7P 304851-31-8P 304851-37-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

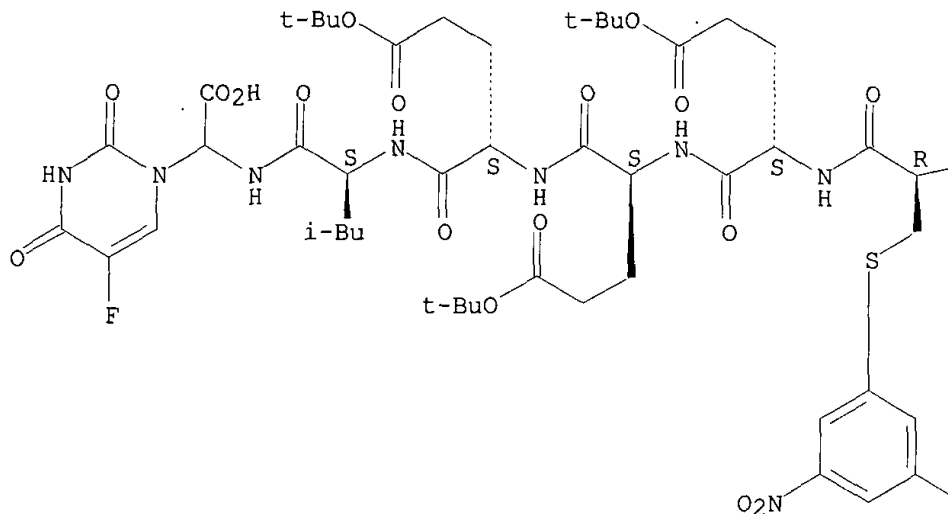
(prepn. of polymeric drug **conjugate** contg. water-sol. polymers and multifunctional chem. moieties and enzymically cleavable linkers and biol. active agents)

RN 304851-30-7 HCAPLUS

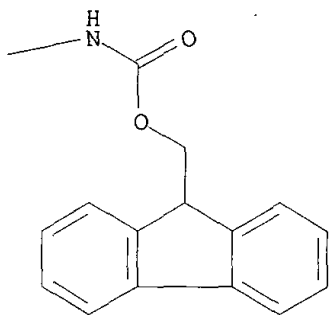
CN Glycine, S-(3,5-dinitrophenyl)-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-cysteinyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-leucyl-2-(5-fluoro-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-, 2,3,4-tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B

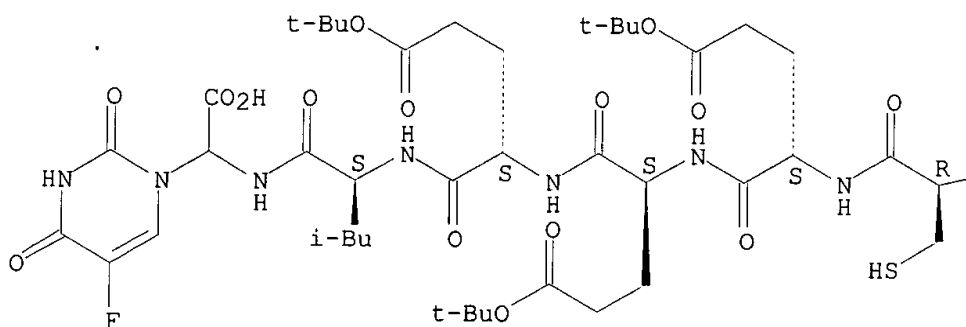
NO₂

RN 304851-31-8 HCAPLUS

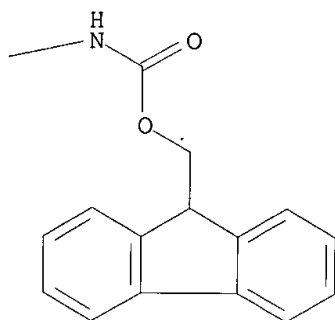
CN Glycine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-cysteinyl-L-.alpha.-
 glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-leucyl-2-(5-fluoro-3,4-
 dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-, 2,3,4-tris(1,1-dimethylethyl) ester
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



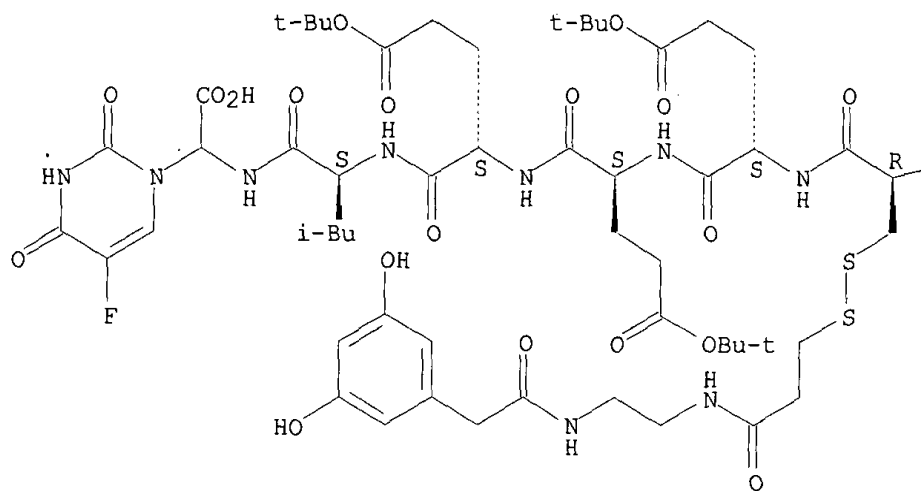
PAGE 1-B



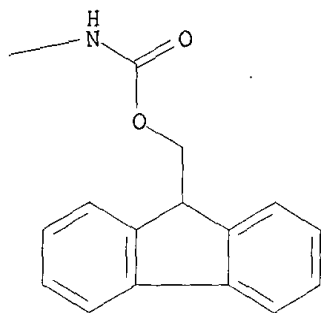
RN 304851-37-4 HCAPLUS
 CN Glycine, 3-[[3-[[2-[[[(3,5-dihydroxyphenyl)acetyl]amino]ethyl]amino]-3-oxopropyl]dithio]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-leucyl-2-(5-fluoro-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-, 2,3,4-tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:458458 HCAPLUS

DOCUMENT NUMBER: 133:238288

TITLE: A novel synthesis of oligonucleotide-peptide
conjugates with a base-labile phosphate linker between
the two components according to the allyl-protected
phosphoramidite strategy

AUTHOR(S): Sakakura, Akira; Hayakawa, Yoshihiro

CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, Graduate School of
Human Informatics, Nagoya University, Nagoya,
464-8601, Japan

SOURCE: Tetrahedron (2000), 56(26), 4427-4435

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:238288

AB An efficient synthesis of base-labile nucleotide-peptide conjugates was accomplished, in which the two components are directly linked between the terminal OH of a nucleotide and the OH of a serine or threonine residue of a peptide by a phosphodiester bond. This synthesis utilizes the phosphoramidite method with allyl for the phosphate linkages and the C-terminus of the peptide, and allyloxycarbonyl for the nucleoside bases and the N-terminus of the peptide. The removal of the allylic protecting groups and the detachment of the products was achieved under non-basic or mild basic conditions without conspicuous decompn. of the labile phosphate linker, and thus, the target conjugates were obtained at a high purity and in high yields.

IT 292177-58-3P 292177-59-4P

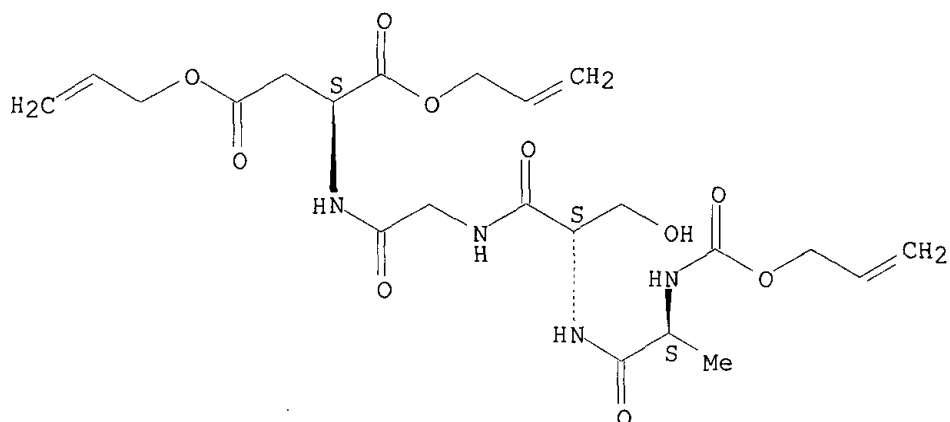
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of oligonucleotide-peptide **conjugates** with phosphate linker by phosphoramidite strategy)

RN 292177-58-3 HCAPLUS

CN L-Aspartic acid, N-[(2-propenyloxy)carbonyl]-L-alanyl-L-serylglycyl-, di-2-propenyl ester (9CI) (CA INDEX NAME)

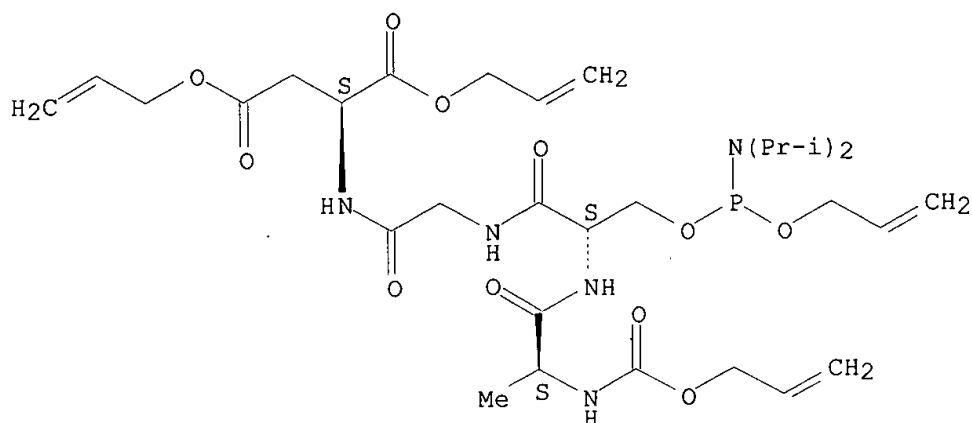
Absolute stereochemistry.



RN 292177-59-4 HCAPLUS

CN L-Aspartic acid, N-[(2-propenyloxy)carbonyl]-L-alanyl-O-[[bis(1-methylethyl)amino](2-propenyloxy)phosphino]-L-serylglycyl-, di-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:487221 HCAPLUS

DOCUMENT NUMBER: 131:130287

TITLE: Chemical derivatives of autoantigens and autoimmune-suppressive peptides and pharmaceutical composition containing the same

INVENTOR(S): Bai, Jane Pei-Fan

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 9937315 | A1 | 19990729 | WO 1999-US1884 | 19990127 |
| W: AU, BR, CA, CN, IL, JP, MX, RU | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9925667 | A1 | 19990809 | AU 1999-25667 | 19990127 |
| PRIORITY APPLN. INFO.: | | | US 1998-72702P | P 19980127 |
| | | | US 1998-90677P | P 19980625 |
| | | | US 1998-104663P | P 19981016 |
| | | | WO 1999-US1884 | W 19990127 |

AB Compds. are disclosed in which autoantigen, analogs of said autoantigen, peptide fragments of said autoantigen, and analogs of said peptide are chem. conjugated to fatty acids in various forms. Such derivs. effectively modulate the immune responses in an autoantigen-specific way and are therefore useful for autoimmune diseases, such as juvenile diabetes, multiple sclerosis, rheumatoid arthritis, and many others.

IT **233660-48-5DP**, polyethylene glycol-PS resin **conjugates**

RL: PNU (Preparation, unclassified); PRP (Properties); RCT (Reactant);

PREP (Preparation)

(chem. derivs. of autoantigens and autoimmune-suppressive peptides for therapeutic use)

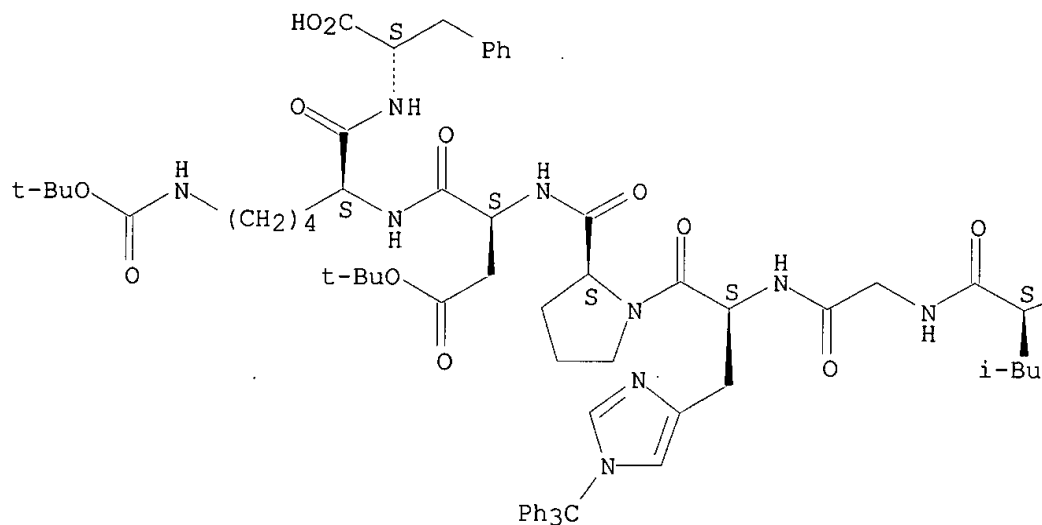
RN 233660-48-5 HCAPLUS

CN L-Phenylalanine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-1-(triphenylmethyl)-

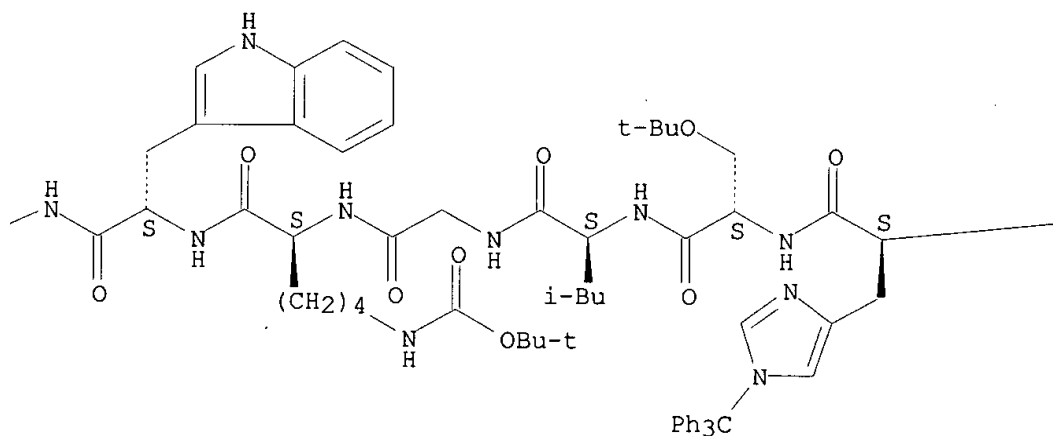
L-histidyl-O-(1,1-dimethylethyl)-L-seryl-L-leucylglycyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-tryptophyl-L-leucylglycyl-1-(triphenylmethyl)-L-histidyl-L-prolyl-L-.alpha.-aspartyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-, 11-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

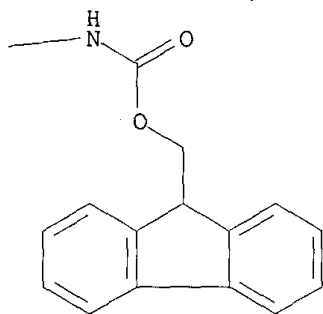
Absolute stereochemistry.

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PAGE 1-B





REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:133618 HCAPLUS

DOCUMENT NUMBER: 130:187175

TITLE: Conjugates targeted to the interleukin-2 receptor

INVENTOR(S): Prakash, Ramesh K.

PATENT ASSIGNEE(S): Theratech, Inc., USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|--|-----------------|------------|
| WO 9907324 | A2 | 19990218 | WO 1998-US16290 | 19980805 |
| WO 9907324 | A3 | 19990415 | | |
| W: | | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | |
| RW: | | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | |
| EP 1011705 | A2 | 20000628 | EP 1998-939226 | 19980805 |
| R: | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | |
| ZA 9807181 | A | 19990323 | ZA 1998-7181 | 19980811 |
| PRIORITY APPLN. INFO.: | | | US 1997-914042 | A 19970805 |
| | | | WO 1998-US16290 | W 19980805 |
| AB | | A compn. for intracellular delivery of a chem. agent into an interleukin-2-receptor-bearing cell, e.g. an activated T cell, includes a | | |

chem. agent and at least two copies of an interleukin-2-receptor-binding and endocytosis-inducing ligand coupled to a water sol. polymer. The ligand binds to a receptor on the interleukin-2-receptor-bearing cell and elicits endocytosis of the compn. The compn. also optionally includes a spacer for coupling the chem. agent and the ligand to the polymer. Chem. agents can include cytotoxins, transforming nucleic acids, gene regulators, labels, antigens, drugs, and the like. A preferred water sol. polymer is polyalkylene oxide, such as polyethylene glycol and polyethylene oxide, and activated derivs. thereof. The compn. can further comprise a carrier such as another water sol. polymer, liposome, or particulate. Methods of using these compns. for delivering a chem. agent in vivo or in vitro are also disclosed.

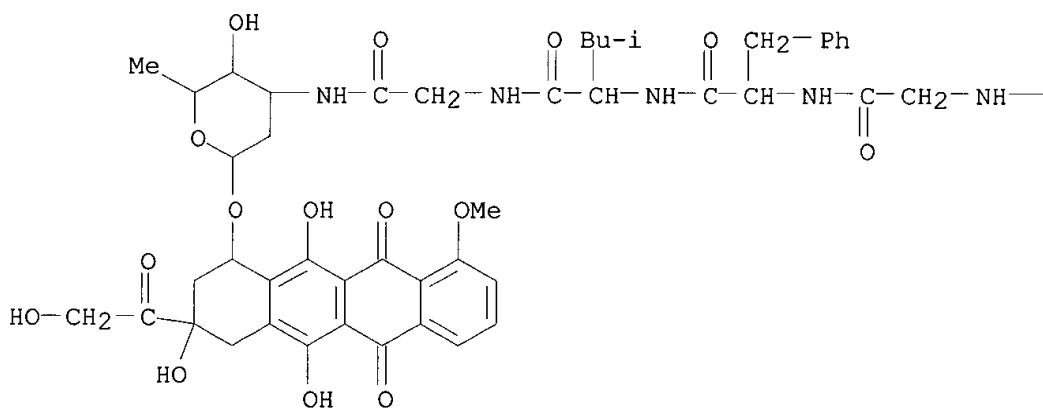
IT 220680-39-7P

RL: BAC (Biological activity or effector, except adverse); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates targeted to the interleukin-2 receptor)

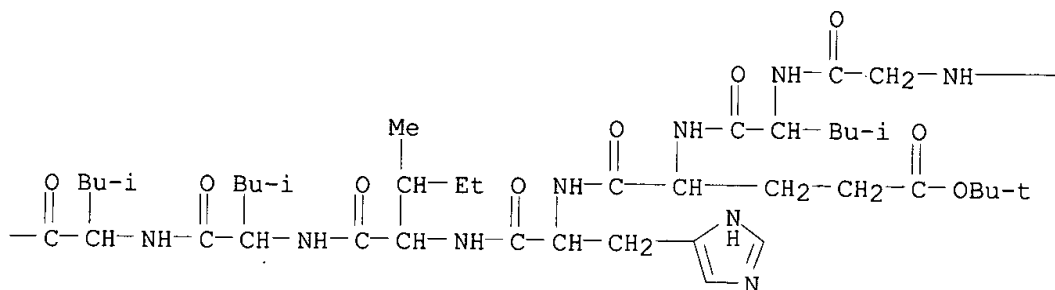
RN 220680-39-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy-, 1-ether with (8S,10S)-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(2-hydroxyethyl)glycyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-isoleucyl-L-leucyl-L-leucylglycyl-L-phenylalanyl-L-leucylglycyl]amino]-.alpha.-L-lyxo-hexopyranosyl]oxy]-5,12-naphthacenedione 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

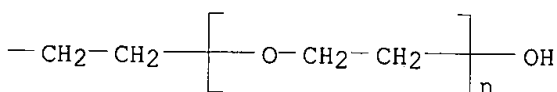
PAGE 1-A



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PAGE 1-C



L24 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:1383 HCAPLUS

DOCUMENT NUMBER: 128:61804

TITLE: aPL immunoreactive peptides and their conjugates for treatment of aPL antibody-mediated pathologies

INVENTOR(S): Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin

PATENT ASSIGNEE(S): Lajolla Pharmaceutical Company, USA; Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin

SOURCE: PCT Int. Appl., 155 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 9746251 | A1 | 19971211 | WO 1997-US10075 | 19970606 |
| W: | AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| US 6207160 | B1 | 20010327 | US 1996-660092 | 19960606 |
| AU 9736404 | A1 | 19980105 | AU 1997-36404 | 19970606 |
| AU 734638 | B2 | 20010621 | | |
| EP 954531 | A1 | 19991110 | EP 1997-933138 | 19970606 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| JP 2000512981 | T2 | 20001003 | JP 1998-500927 | 19970606 |
| NO 9805636 | A | 19990208 | NO 1998-5636 | 19981203 |

PRIORITY APPLN. INFO.:

US 1996-660092 A2 19960606
 US 1996-760508 A 19961205
 US 1995-482651 A2 19950607
 WO 1997-US10075 W 19970606

AB APL analogs that bind specifically to B cells to which an aPL epitope binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Conjugates comprising aPL analogs and nonimmunogenic valency platform mols. are provided as are novel nonimmunogenic valency platform mols. and linkers. Methods of prepg. and identifying said analogs, methods of treatment using said analogs, methods and compns. for prepg. conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

IT 200291-34-5P

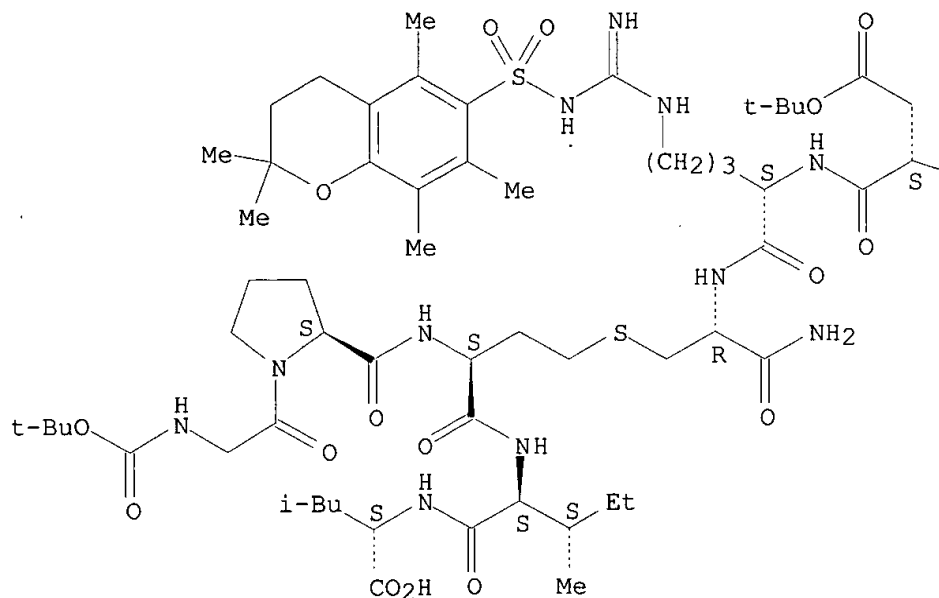
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (aPL immunoreactive peptides and their **conjugates** for treatment of aPL antibody-mediated pathologies)

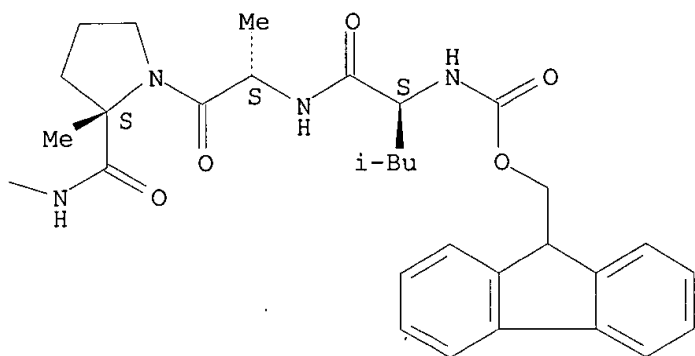
RN 200291-34-5 HCAPLUS

CN L-Cysteinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-leucyl-L-alanyl-2-methyl-L-prolyl-L-.alpha.-aspartyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-, 1,1-dimethylethyl ester, (6.fwdarw.3')-thioether with N-[(1,1-dimethylethoxy)carbonyl]glycyl-L-prolyl-L-homocysteiny-L-isoleucyl-L-leucine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L24 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:633658 HCAPLUS

DOCUMENT NUMBER: 127:293529

TITLE: Synthesis and structural characterization of conjugates of adenosine and tetra-aspartate, novel analogs of ATP

AUTHOR(S): Pehk, Tonis; Uri, Asko

CORPORATE SOURCE: Inst. Chemical Physics and Biophysics, Tallinn, EE0026, Estonia

SOURCE: Bioorg. Med. Chem. Lett. (1997), 7(17), 2159-2164
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Solid phase synthesis of conjugates of adenosine and tetra-aspartate, potential ligands of P2 (ATP) receptors, is described. Different spatial arrangement of the peptide chain relative to the adenosine moiety in these highly charged compds. is shown by 1H and 13C NMR spectroscopy. PKa values for the three internal aspartates and adenine base were detd.

IT 196945-02-5D, resin bound

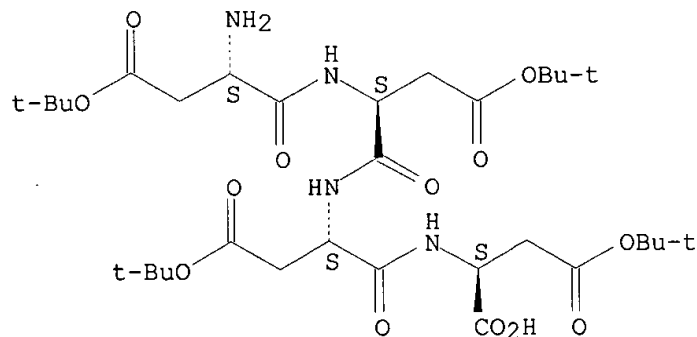
RL: RCT (Reactant)

(prepn. and structural characterization of **conjugates** of adenosine and tetra-aspartate, novel analogs of ATP)

RN 196945-02-5 HCAPLUS

CN L-Aspartic acid, L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-, 1,2,3,4-tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:440179 HCAPLUS

DOCUMENT NUMBER: 127:51009

TITLE: Peptide conjugates derived from thymic hormones and their compositions for use as drugs

INVENTOR(S): Dussourd, D'hinterland Lucien; Pinel, Anne-Marie

PATENT ASSIGNEE(S): Societe D'etude Et De Recherche De Pathologie Appliquee - Serpa, Fr.; Dussourd D'hinterland, Lucien; Pinel, Anne-Marie

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9718239 | A1 | 19970522 | WO 1996-FR1812 | 19961115 |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| FR 2741076 | A1 | 19970516 | FR 1995-13544 | 19951115 |
| FR 2741076 | B1 | 19980130 | | |
| CA 2237995 | AA | 19970522 | CA 1996-2237995 | 19961115 |
| AU 9676832 | A1 | 19970605 | AU 1996-76832 | 19961115 |
| EP 861266 | A1 | 19980902 | EP 1996-939132 | 19961115 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000500447 | T2 | 20000118 | JP 1997-518639 | 19961115 |
| US 6211155 | B1 | 20010403 | US 1998-68767 | 19980824 |
| PRIORITY APPLN. INFO.: | | | FR 1995-13544 | A 19951115 |
| | | | WO 1996-FR1812 | W 19961115 |

OTHER SOURCE(S): MARPAT 127:51009

AB Peptide conjugates have been synthesized which have a sequence of at least 3 amino acids derived from a thymic hormone selected from thymuline and thymopoietine (the amino acids are in the D, L, or DL form) and in which the sequence is conjugated to a mono- or dicarboxylic acid. The peptide conjugates are used in pharmaceutical or cosmetic compns. Thus, Ac-Pyro-Ala-Lys-Ser-Gln-Gly-Gly-Ser-Asn-NH₂ was prepd. and tested in regards to cellular activity.

IT **191221-06-4P**

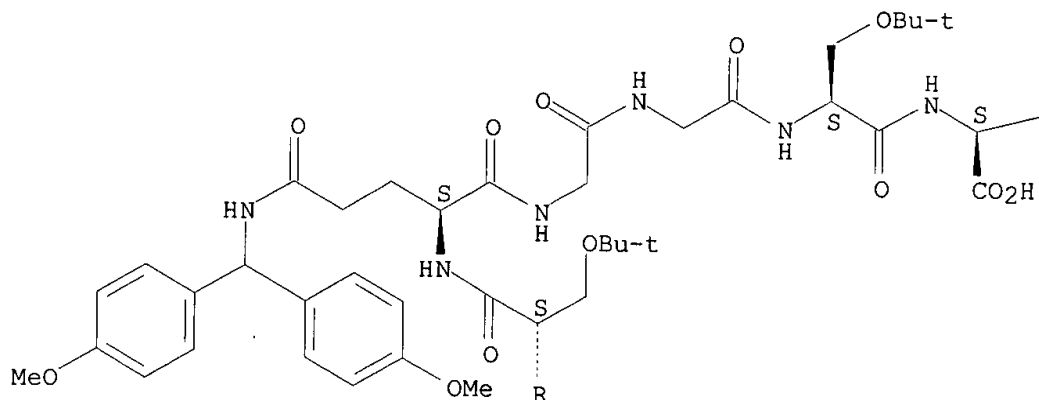
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(peptide **conjugates** derived from thymic hormones and their compns. for use as drugs)

RN 191221-06-4 HCAPLUS

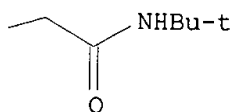
CN 2-9-Thymulin (swine peptide moiety), 3-[N⁶-[(1,1-dimethylethoxy)carbonyl]-L-lysine]-4-[O-(1,1-dimethylethyl)-L-serine]-5-[N-[bis(4-methoxyphenyl)methyl]-L-glutamine]-8-[O-(1,1-dimethylethyl)-L-serine]-9-[N-(1,1-dimethylethyl)-L-asparagine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

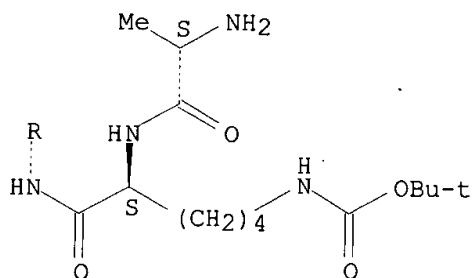
PAGE 1-A



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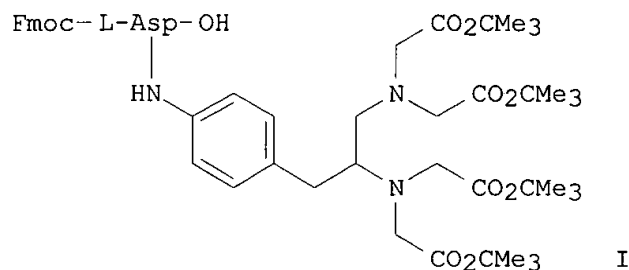


PAGE 2-A



L24 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:154992 HCAPLUS
 DOCUMENT NUMBER: 126:199815
 TITLE: Synthesis of an Amino Acid Analog To Incorporate
 p-Aminobenzyl-EDTA in Peptides
 AUTHOR(S): Song, Anne In.; Rana, Tariq M.
 CORPORATE SOURCE: Department of Pharmacology Robert Wood Johnson Medical
 School, University of Medicine and Dentistry of New
 Jersey, Piscataway, NJ, 08854, USA
 SOURCE: Bioconjugate Chem. (1997), 8(2), 249-252.
 CODEN: BCCHE; ISSN: 1043-1802
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 126:199815
 GI



AB A convenient and straightforward synthesis of an amino acid analog I (Fmoc = 9-fluorenylmethoxycarbonyl), compatible with Fmoc solid phase peptide synthesis strategy is described. I was used to incorporate p-aminobenzyl-EDTA at an internal sequence position in an HIV-1 Tat protein fragment. After cleavage from the resin and std. deprotection, the peptide was purified by high-performance liq. chromatog. and characterized by mass spectrometry. Through this methodol., flexible linkers of different lengths and contg. various structures can be placed between the .alpha.-carbon backbone of peptides and metal chelates. These peptides will provide a new class of affinity cleaving reagents that can be directed against protein and nucleic acid targets.

IT **187671-20-1P**

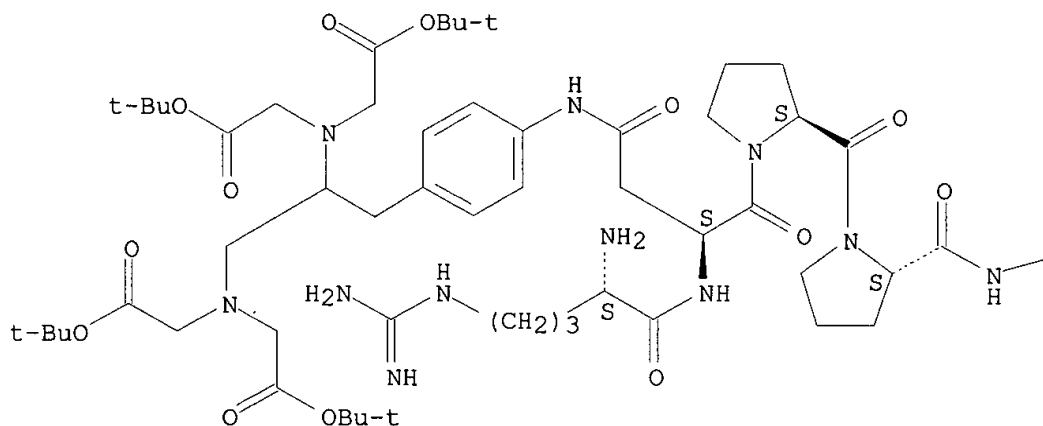
RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of a protected aspartic acid aminobenzyl-EDTA **conjugate**
 for incorporation into peptides)

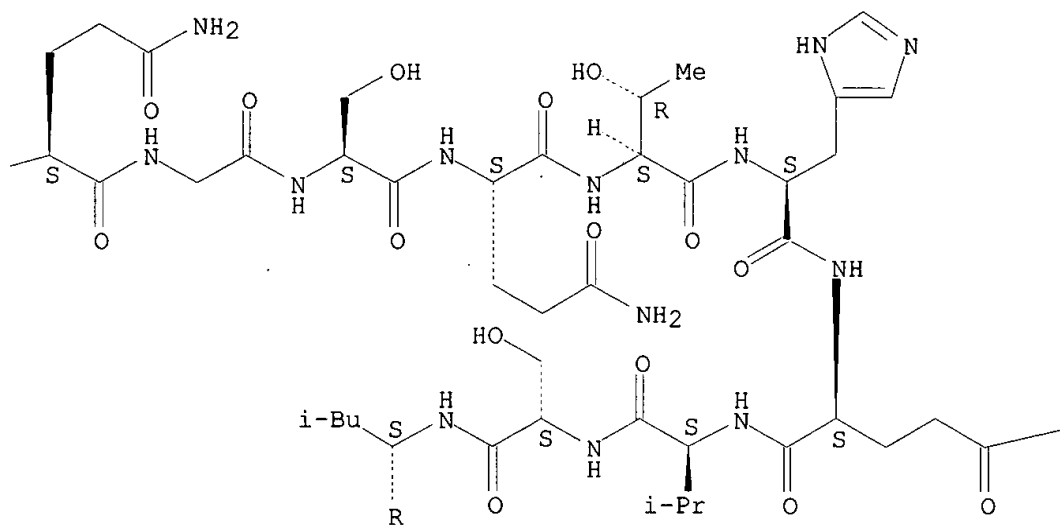
RN 187671-20-1 HCAPLUS

CN L-Glutamine, L-arginyl-N-[4-[2,3-bis[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]propyl]phenyl]-L-asparaginyl-L-prolyl-L-prolyl-L-glutaminyglycyl-L-seryl-L-glutaminy-L-threonyl-L-histidyl-L-glutaminy-L-valyl-L-seryl-L-leucyl-L-seryl-L-lysyl- (9CI) (CA INDEX NAME)

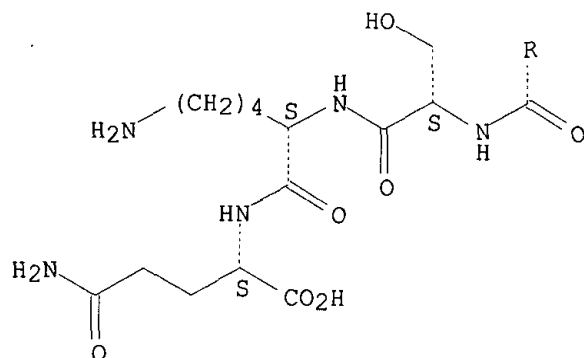
Absolute stereochemistry.

PAGE 1-A





—NH₂



L24 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:718838 HCAPLUS

DOCUMENT NUMBER: 126:89748

TITLE: Design and synthesis of flavin-conjugated peptides and assembly on a gold electrode

AUTHOR(S): Sakamoto, Seiji; Aoyagi, Haruhiko; Nakashima, Naotoshi; Mihara, Hisakazu

CORPORATE SOURCE: Dep. Applied Chem., Fac. Eng., Nagasaki Univ., Nagasaki, 852, Japan

SOURCE: J. Chem. Soc., Perkin Trans. 2 (1996), (11), 2319-2326
CODEN: JCPKBH; ISSN: 0300-9580

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Flavin-conjugated peptides composed of one or two amphiphilic .alpha.-helix segments have been designed and synthesized. 7-Acetyl-10-methylisoalloxazine (Fla) as a model flavin has been introduced on the side chain of Cys at the 6th, 7th or 8th position of each .alpha.-helical 14-peptide. A CD study in aq. soln. revealed that the position of Fla on the peptide strongly influenced the peptide secondary structure. Addnl., CD spectra indicated that the Fla in the peptides was oriented in a different manner depending on the position when the peptide took on the .alpha.-helix structure. Furthermore, the flavin-conjugated peptides have been adsorbed on a gold surface through the sulfide linkage, as a basic study for peptidyl devices in the future. By the use of FLA as an electrochem. probe, we examd. properties of the peptide assembled on the gold electrode. The cyclic voltammetry measurements revealed that the functional group, Fla, was redox-active on the electrode and the peptide bound on the surface in a monolayer. Moreover, the flavin-conjugated peptide could mediate the electron transfer from the electrode to Fe(CN)₆³⁻ ion or cytochrome c in a vector manner. The redox-active probe, Fla, has been demonstrated to provide significant information about the assembly and function of the .alpha.-helix peptides on the gold electrode surface by electrochem. measurements.

IT 185458-33-7DP, resin-bound 185458-34-8DP, resin-bound
185458-35-9DP, resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(design and synthesis of flavin-conjugated peptides and assembly on gold electrode)

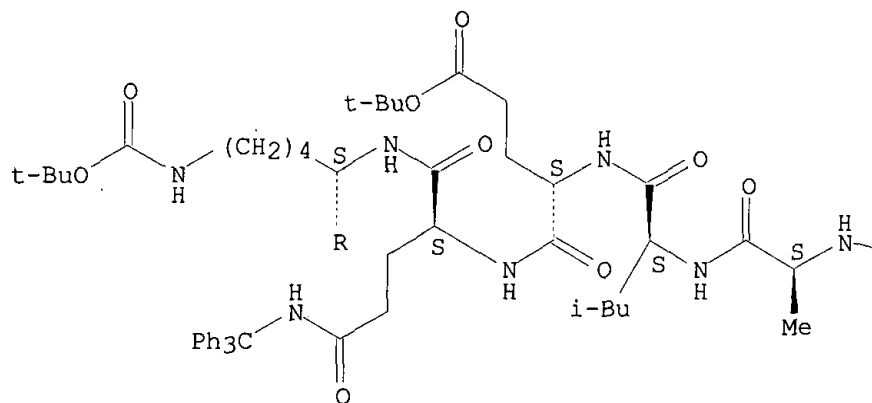
RN 185458-33-7 HCAPLUS

CN L-Cysteinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-alanyl-L-leucyl-L-

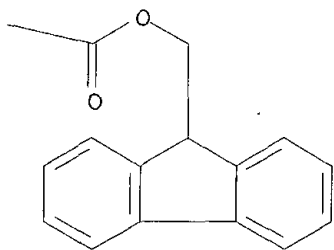
.alpha.-glutamyl-N-(triphenylmethyl)-L-glutaminyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-S-(triphenylmethyl)-L-cysteinyl-L-alanyl-L-alanyl-L-leucyl-L-.alpha.-glutamyl-N-(triphenylmethyl)-L-glutaminyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-leucyl-L-alanyl-.beta.-alanyl-S-[(acetylamino)methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

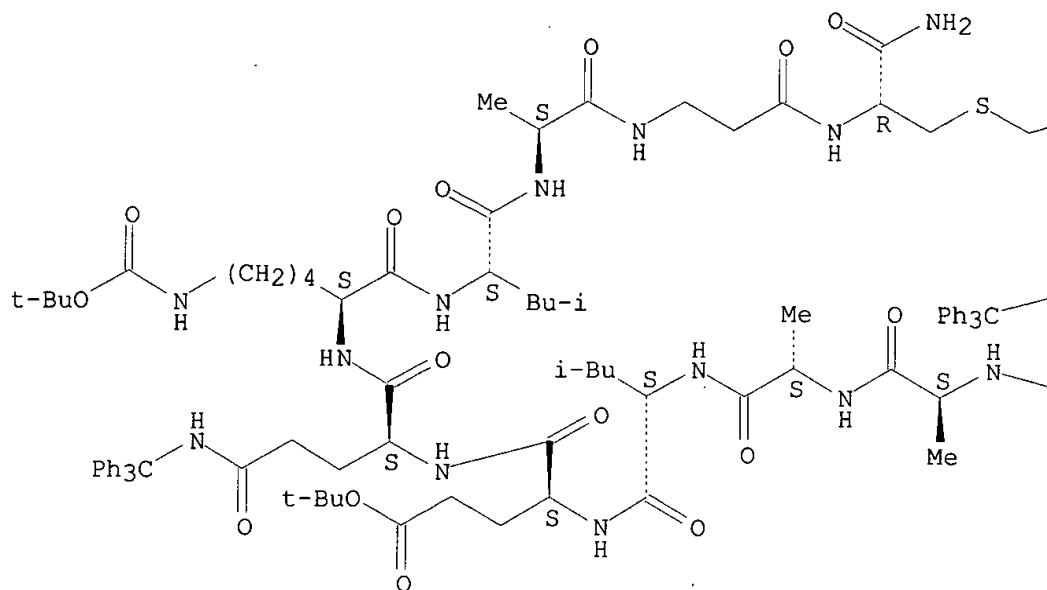
PAGE 1-A



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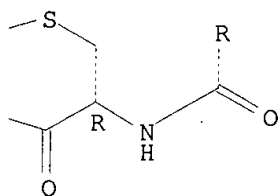


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PAGE 2-B

NHAc

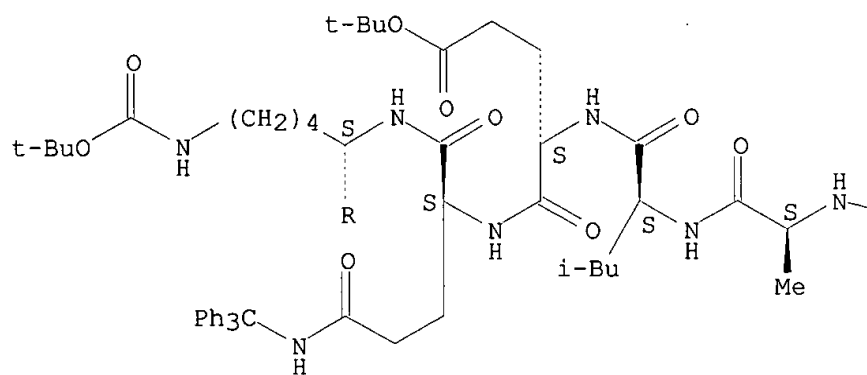


RN 185458-34-8 HCAPLUS

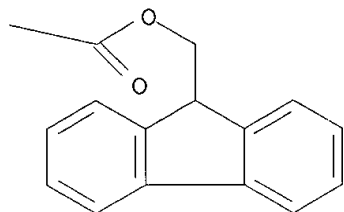
CN L-Cysteinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-alanyl-L-leucyl-L-.alpha.-glutamyl-N-(triphenylmethyl)-L-glutamyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-leucyl-S-(triphenylmethyl)-L-cysteinyl-L-alanyl-L-leucyl-L-.alpha.-glutamyl-N-(triphenylmethyl)-L-glutamyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-leucyl-L-alanyl-.beta.-alanyl-S-[(acetylamino)methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

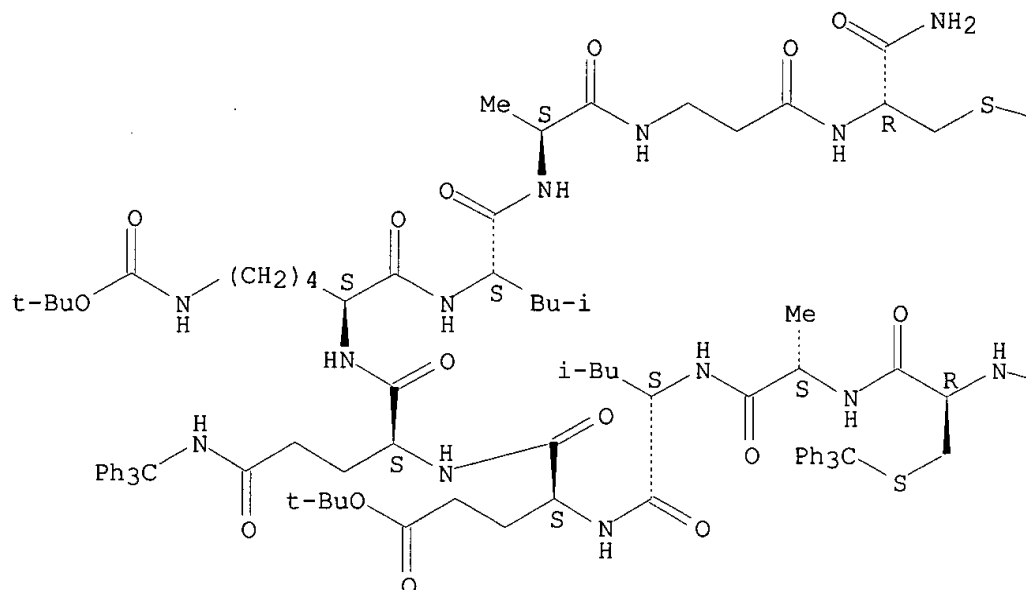
PAGE 1-A



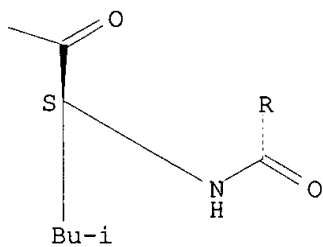
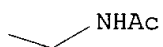
PAGE 1-B



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PAGE 2-B



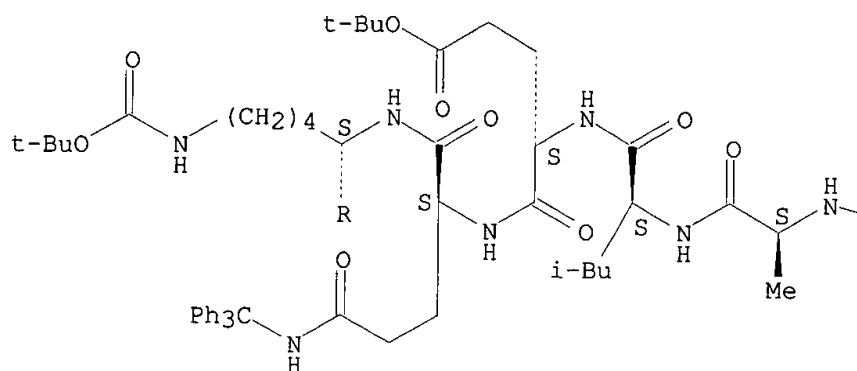
RN 185458-35-9 HCAPLUS

CN L-Cysteinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-alanyl-L-leucyl-L-.alpha.-glutamyl-N-(triphenylmethyl)-L-glutamyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-leucyl-L-alanyl-S-(triphenylmethyl)-L-cysteinyl-L-leucyl-L-.alpha.-glutamyl-N-(triphenylmethyl)-L-glutamyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-leucyl-L-alanyl-.beta.-alanyl-S-[(acetylamino)methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX

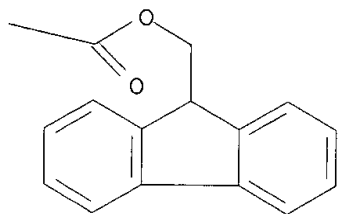
NAME)

Absolute stereochemistry.

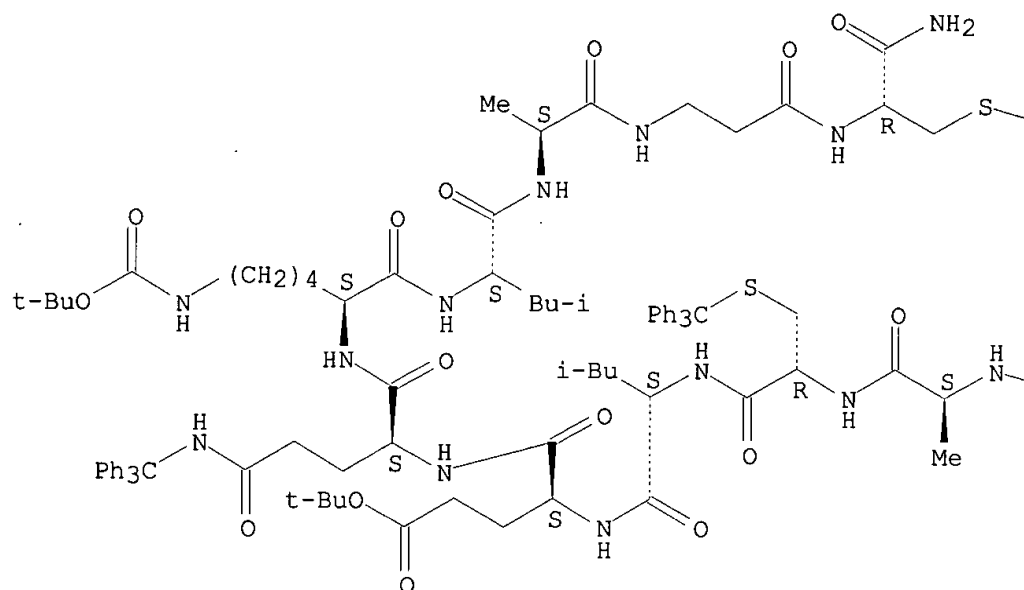
PAGE 1-A



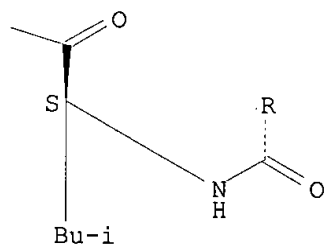
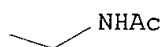
PAGE 1-B



PAGE 2-A



PAGE 2-B



L24 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:350538 HCAPLUS

DOCUMENT NUMBER: 125:49330

TITLE: Polypeptides derived from major histocompatibility complex class I antigen for treatment of diabetes mellitus

INVENTOR(S): Mapelli, Claudio; Meyers, Chester A.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
 SOURCE: U.S., 8 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------------|------|----------|-----------------|----------|
| | US 5516642 | A | 19960514 | US 1992-976872 | 19921116 |

OTHER SOURCE(S): MARPAT 125:49330

AB Chem. modified peptides (Markush given) derived from MHC class I antigens are described for use in the treatment of diabetes mellitus. These peptides are more effective than prior art MHC I peptides, are more stable in bioassays, do not aggregate or form gels and can be radioiodinated with retention of activity.

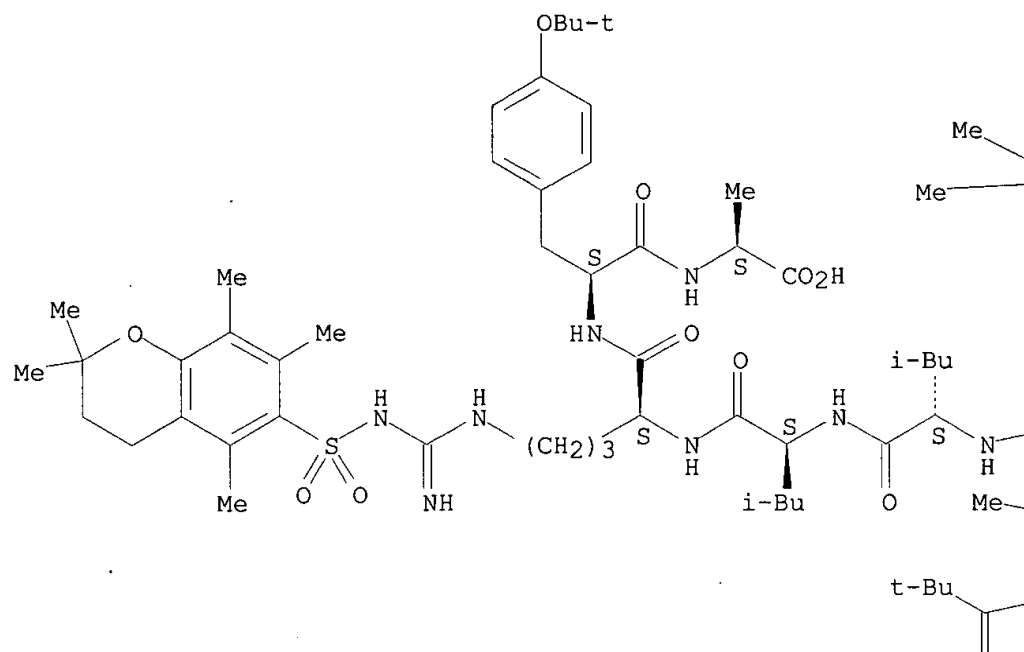
IT **178177-12-3DP, resin conjugates**
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (polypeptides derived from major histocompatibility complex class I antigen for treatment of diabetes mellitus)

RN 178177-12-3 HCAPLUS

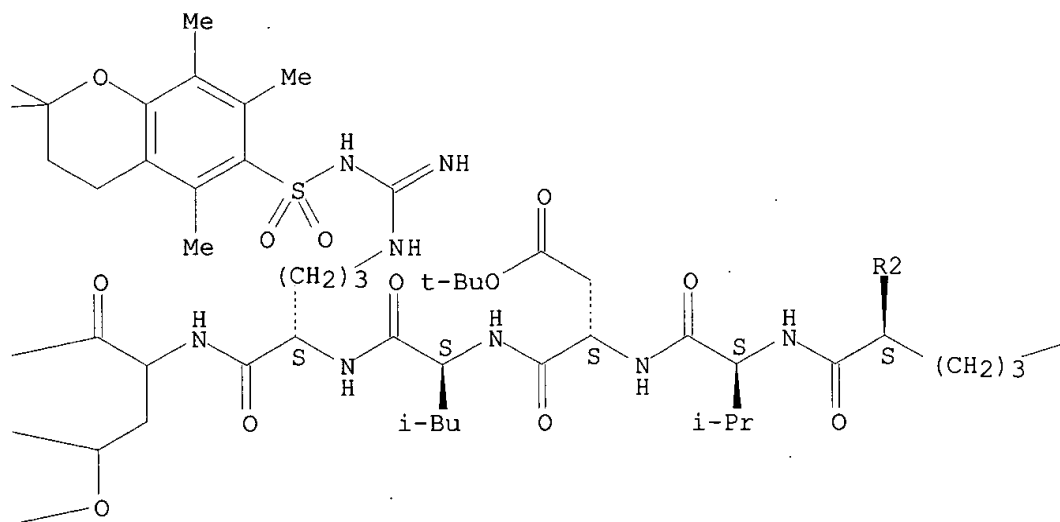
CN L-Alanine, glycyl-L-asparaginy-L-.alpha.-glutamyl-L-glutaminyl-O-(1,1-dimethylethyl)-L-seryl-L-phenylalanyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-valyl-L-.alpha.-aspartyl-L-leucyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-4-(2,2-dimethyl-1-oxopropoxy)norvalyl-L-leucyl-L-leucyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-O-(1,1-dimethylethyl)-L-tyrosyl-, 3,9-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

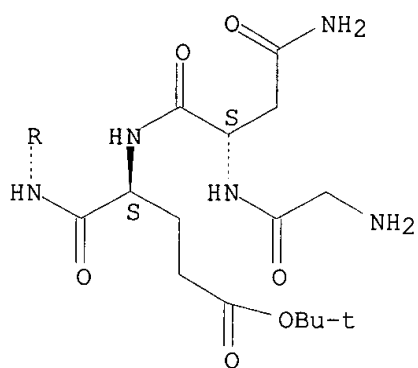
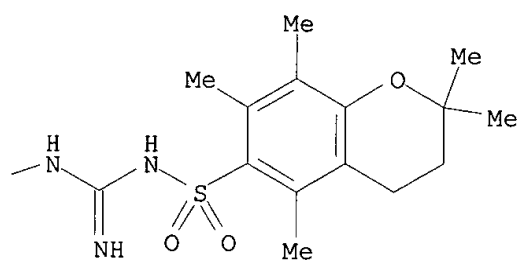
Absolute stereochemistry.

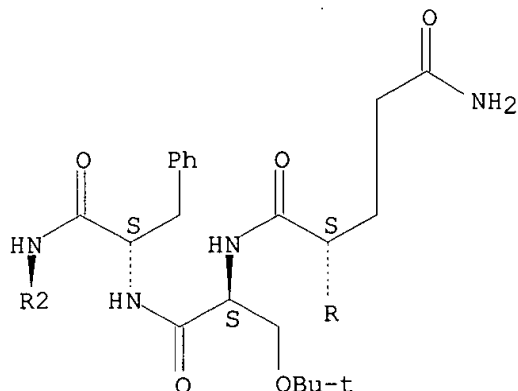
PAGE 1-A



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L24 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:27001 HCAPLUS

DOCUMENT NUMBER: 124:203074

TITLE: Amino acids and peptides. XXV. Preparation of
fibronectin-related peptide poly(ethylene glycol)
hybrids and their inhibitory effect on experimental
metastasis

AUTHOR(S): Kawasaki, Koichi; Namikawa, Machiko; Yamashiro, Yuko;
Iwai, Yuji; Hama, Takao; Tsutsumi, Yasuo; Yamamoto,
Susumu; Nakagawa, Shinsaku; Mayumi, Tadanori

CORPORATE SOURCE: Fac. Pharmaceutical Sciences, Kobe Gakuin Univ., Kobe,
651-21, Japan

SOURCE: Chem. Pharm. Bull. (1995), 43(12), 2133-8
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hybrids of fibronectin-related peptides [Arg-Gly-Asp (RGD),
Arg-Gly-Asp-Ser (RGDS)] and poly(ethylene glycol) (PEG) were prepd. and
their inhibitory effects on exptl. metastasis in mice were examd. The
inhibitory effect of RGD was markedly potentiated by hybrid formation with
poly(ethylene glycol) 6000. As to inhibitory effect, RGD was more potent
than RGDS and RGD PEG hybrids were superior to RGDS PEG hybrids. Hybrid
formation with PEG 6000 was more effective than that with PEG 4000.

IT 174276-48-3P

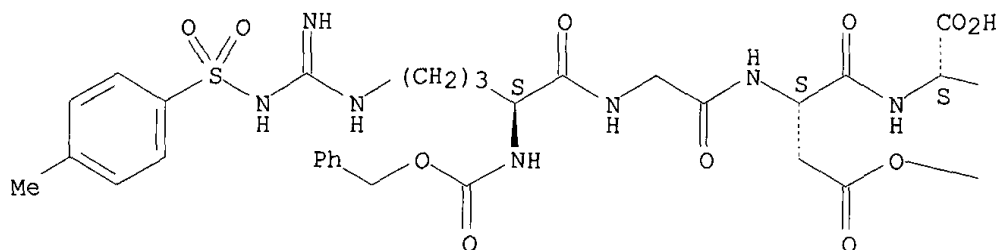
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antitumor activity of peptide-polyethylene glycol
conjugates)

RN 174276-48-3 HCAPLUS

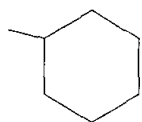
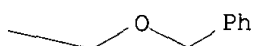
CN L-Serine, N-[N-[N-[N5-[imino[[(4-methylphenyl) sulfonyl] amino] methyl]-N2-
[(phenylmethoxy) carbonyl]-L-ornithyl] glycy]-L-.alpha.-aspartyl]-O-
(phenylmethyl)-, 4-cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

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L24 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:837578 HCAPLUS

DOCUMENT NUMBER: 123:334348

TITLE: Methods for the solid phase synthesis of glycoconjugates

INVENTOR(S): Vetter, Dirk; Tumelty, David; Antonenko, Valery

PATENT ASSIGNEE(S): Affymax Technologies N.V., Neth.

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9518971 | A1 | 19950713 | WO 1995-US484 | 19950110 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9516029 | A1 | 19950801 | AU 1995-16029 | 19950110 |
| PRIORITY APPLN. INFO.: | | | US 1994-179741 | 19940111 |
| | | | US 1994-201607 | 19940225 |
| | | | WO 1995-US484 | 19950110 |

AB An efficient and versatile method of forming N-linked glycoconjugates is described wherein a glycosyl acceptor, typically comprising an activated carboxyl group, is reacted with a glycosylating agent, typically a

glycosyl amine, in the presence of a coupling catalyst and optionally an exogenous base. Depending on the choice of reactive site, this method can be used to form N-linked glycoconjugates, in either a sol. or substrate-bound, linear or branched format.

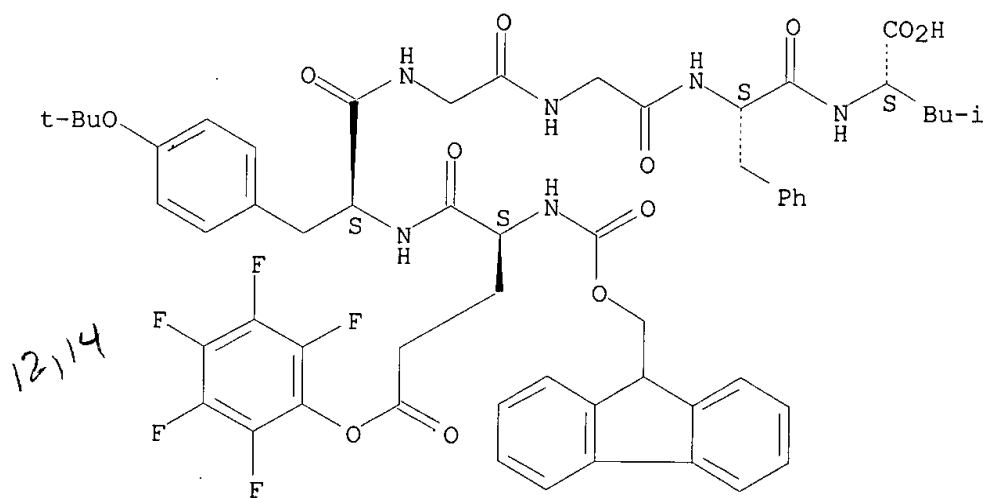
IT **168423-84-5DP**, resin bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(methods for solid-phase synthesis of **glycoconjugates**)

RN 168423-84-5 HCAPLUS

CN L-Leucine, N-[N-[N-[N-[O-(1,1-dimethylethyl)-N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl]-L-tyrosyl]glycyl]glycyl]-L-phenylalanyl]-, 5-(pentafluorophenyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



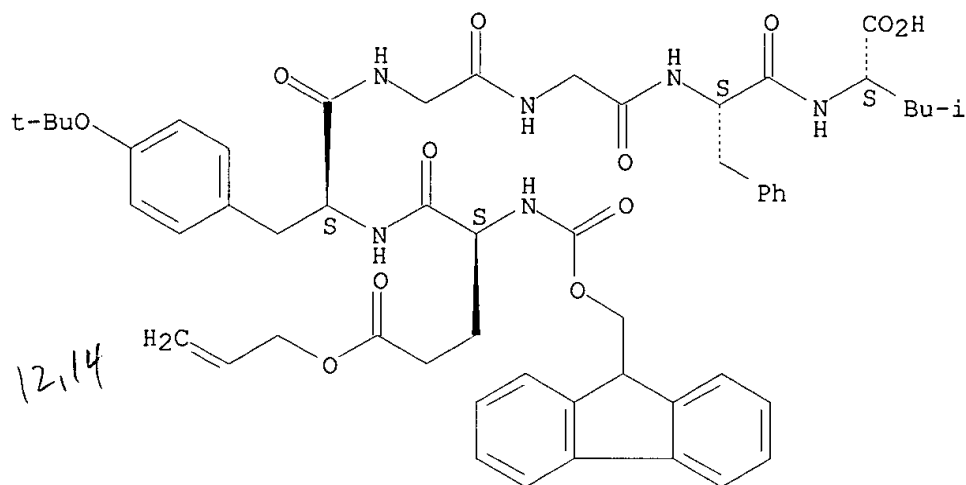
IT **168423-82-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(methods for solid-phase synthesis of **glycoconjugates**)

RN 168423-82-3 HCAPLUS

CN L-Leucine, N-[N-[N-[N-[O-(1,1-dimethylethyl)-N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl]-L-tyrosyl]glycyl]glycyl]-L-phenylalanyl]-, 5-(2-propenyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:729167 HCAPLUS

DOCUMENT NUMBER: 123:103526

TITLE: Amino acid substituted analogs of atrial natriuretic peptides that retains their activity and with specificity for the A receptor

INVENTOR(S): Lowe, David; Cunningham, Brian C.; Oare, David; McDowell, Robert S.; Burnier, John

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

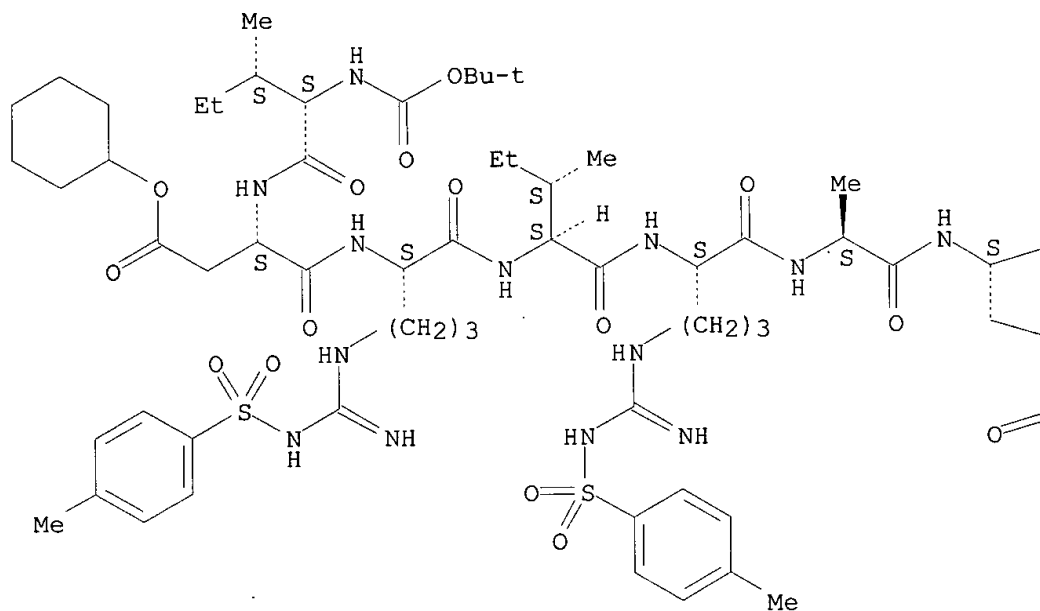
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9513296 | A1 | 19950518 | WO 1994-US12591 | 19941104 |
| W: AU, CA, CN, CZ, JP, NZ, RU, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2174517 | AA | 19950518 | CA 1994-2174517 | 19941104 |
| AU 9519349 | A1 | 19950529 | AU 1995-19349 | 19941104 |
| EP 728147 | A1 | 19960828 | EP 1995-901112 | 19941104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 09505049 | T2 | 19970520 | JP 1994-513878 | 19941104 |
| US 5665704 | A | 19970909 | US 1995-451240 | 19950525 |
| US 5846932 | A | 19981208 | US 1995-470846 | 19950606 |
| PRIORITY APPLN. INFO.: | | | US 1993-152994 | 19931112 |
| | | | WO 1994-US12591 | 19941104 |
| | | | US 1995-362552 | 19950106 |
| | | | US 1995-419877 | 19950411 |

AB Amino acid substituted human receptor selective atrial natriuretic factor variants, esp. G16R, show equal potency and binding affinity for the human A-receptor but have decreased affinity for the human clearance or C-receptor. These ANF variants have natriuretic, diuretic and vasorelaxant activity but have increased metabolic stability, making them suitable for treating congestive heart failure, acute kidney failure and renal hypertension.

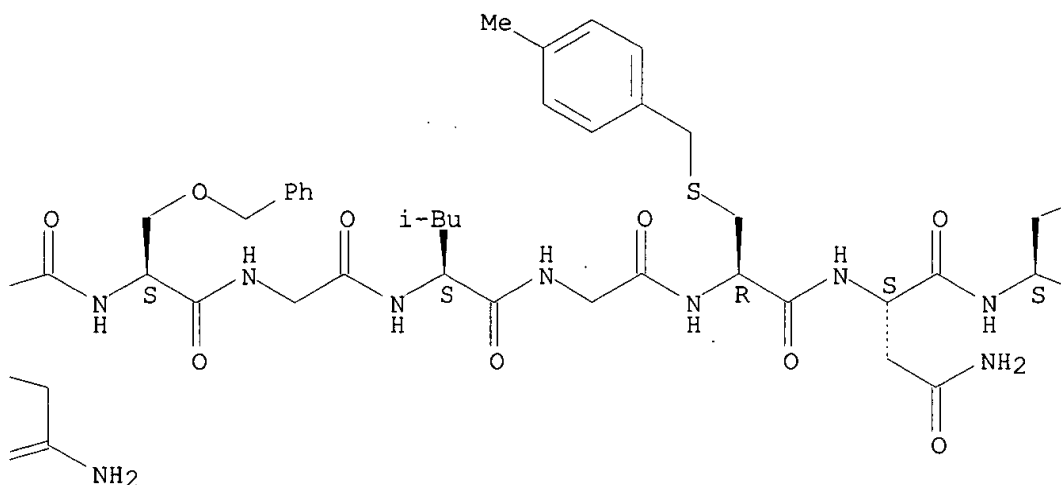
IT **166098-79-9DP, conjugates** with PAM resin
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (atriopectin analog, amino acid sequence; amino acid substituted
 analogs of atrial natriuretic peptides that retains their activity and
 with specificity for receptor)
 RN 166098-79-9 HCAPLUS
 CN 8-24-Atrial natriuretic peptide-24 (rat reduced), N-[(1,1-
 dimethylethoxy)carbonyl]-10-[N5-[imino[[(4-methylphenyl)sulfonyl]amino]met
 hyl]-L-ornithine]-12-[N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-
 ornithine]-15-[O-(phenylmethyl)-L-serine]-19-[S-[(4-methylphenyl)methyl]-L-
 cysteine]-21-[O-(phenylmethyl)-L-serine]-23-[N5-[imino[[(4-
 methylphenyl)sulfonyl]amino]methyl]-L-ornithine]-, 9-cyclohexyl ester,
 (2-bromophenyl)methyl carbonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

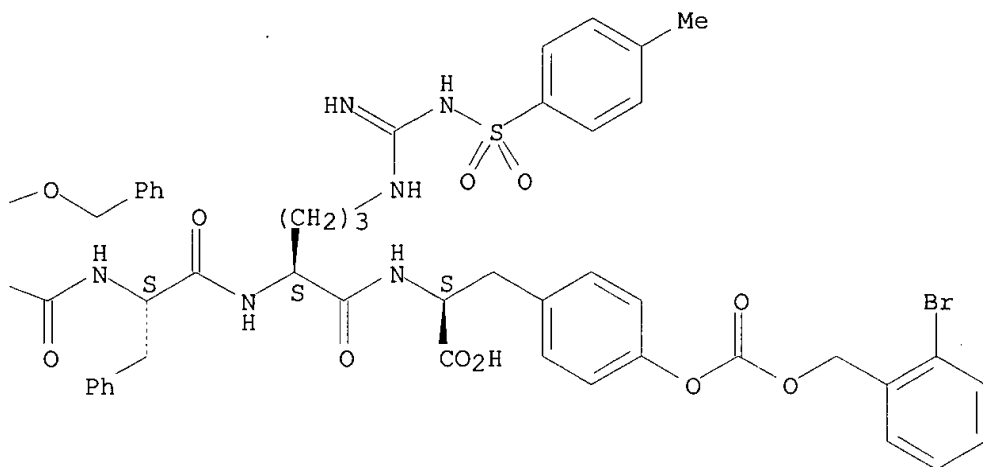
PAGE 1-A



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L24 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:655655 HCAPLUS

DOCUMENT NUMBER: 123:81520

TITLE: Polytuftsins: its possible effects and mechanism during macrophage activation

AUTHOR(S): Dhawan, P.; Nath, I.; Rao, D. N.

CORPORATE SOURCE: Biochemistry and, New, DELHI-110029, India

SOURCE: Immunol. Lett. (1995), 46(1,2), 177-82

CODEN: IMLED6; ISSN: 0165-2478

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polytuftsins (PT) a 35-40 repeat unit of tuftsins (TKPR), when administered as a conjugate with the malarial peptide, ring-infected erythrocyte surface antigen (RESA), enhanced antigen-induced lymphoproliferation and

antibody levels in mice as compared to RESA alone. This enhancement was unrelated to the H-2 background of the animals. The present study was undertaken with a view to understanding the mechanism(s) responsible for this immune enhancement. Peritoneal adherent cells (PAC) from H-2b and H-2d mice were incubated with RESA alone, PT-conjugated RESA, a phys. mixt. of RESA+PT and PT alone. They were subsequently evaluated for I-A expression using monoclonal antibodies and flow cytometry as well as cell-ELISA. Significant increase in I-A expression on PAC was obsd. in all 4 groups as compared to untreated cells. Whereas cells treated with PT-conjugated RESA showed highly significant increase in I-A ($P < 0.001$), the other groups showed moderate increase ($P < 0.05$). This enhancement was attributable to increase in the no. of I-A-pos. cells rather than I-A mols. per cell. Moreover, IL-1 release, as assayed by bioassay, was significantly higher in cells treated with conjugated RESA as compared to cells treated with RESA or PT alone ($P < 0.05$). Thus, it would appear that PT-conjugated RESA peptide of the malarial antigen selectively enhances major histocompatibility complex (MHC) class II mols. on antigen-presenting cells (APC) and may therefore improve immune functions by stimulating better antigen presentation and proliferation of T cells.

IT 116470-02-1D, conjugate with polytuftsins

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

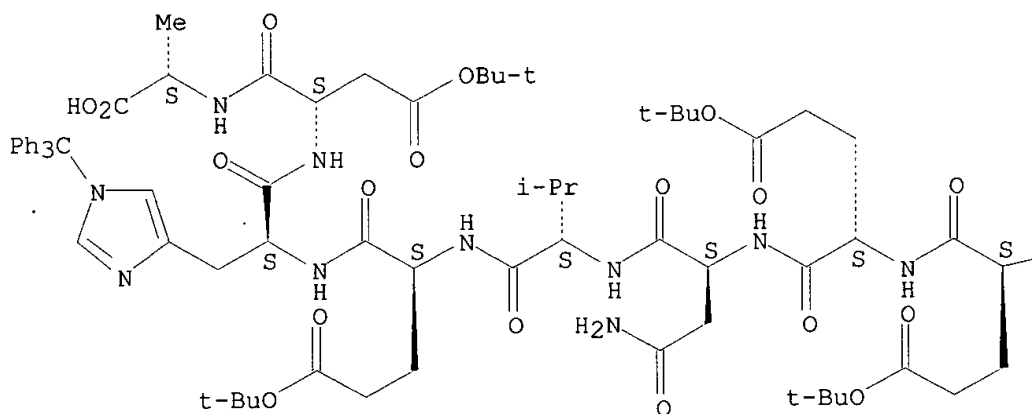
(macrophage activation by polytuftsins-RESA antigen peptide conjugates)

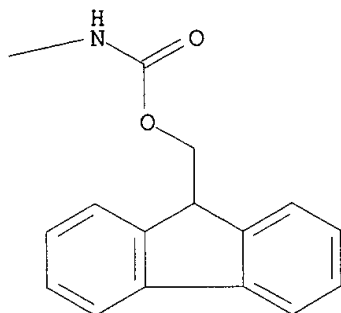
RN 116470-02-1 HCAPLUS

CN L-Alanine, N-[N-[N-[N-[N-[N2-[N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-glutamyl]-L-.alpha.-glutamyl]-L-asparaginyl]-L-valyl]-L-.alpha.-glutamyl]-1-(triphenylmethyl)-L-histidyl]-L-.alpha.-aspartyl]-, 4,5,5',5''-tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L24 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:627362 HCAPLUS

DOCUMENT NUMBER: 121:227362

TITLE: A new inhibitor of the chymotrypsin-like activity of the multicatalytic proteinase complex (20S proteasome) induces accumulation of ubiquitin-protein conjugates in a neuronal cell

AUTHOR(S): Figueiredo-Pereira, Maria E.; Berg, Kelly A.; Wilk, Sherwin

CORPORATE SOURCE: Mount Sinai Sch. Med., CUNY, New York, NY, USA

SOURCE: J. Neurochem. (1994), 63(4), 1578-81

CODEN: JONRA9; ISSN: 0022-3042

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Exposure of HT4 cells (a mouse neuronal cell line) to a new potent permeable peptidyl aldehyde inhibitor of the chymotrypsin-like activity of the multicatalytic proteinase complex (MPC) causes accumulation of ubiquitinated proteins. In contrast, inhibition of calpain or treatment with a lysosomotropic agent failed to produce detectable ubiquitin-protein conjugates. The appearance of such conjugates is not a nonspecific phenomenon because incubation with the peptidyl alc. analog of the inhibitor does not produce accumulation of ubiquitinated proteins. The MPC inhibitor may therefore be a useful tool for identification and study of physiol. pathways involving MPC. Furthermore, the inhibitor may help develop a model for the study of neurodegeneration where accumulation of ubiquitin-protein conjugates is commonly detected in abnormal brain inclusions.

IT 158442-41-2

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

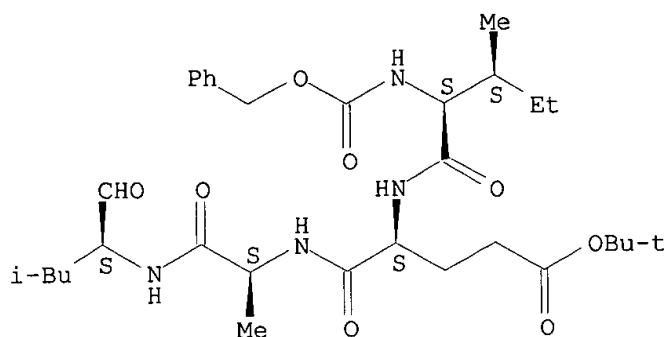
(a new inhibitor of the chymotrypsin-like activity of the multicatalytic proteinase complex (20S proteasome) induces accumulation of ubiquitin-protein **conjugates** in a neuronal cell)

RN 158442-41-2 HCAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-α-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



L24 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:473891 HCAPLUS

DOCUMENT NUMBER: 121:73891

TITLE: Peptide derivatives corresponding to the carboxy terminal sequence of hirudin

INVENTOR(S): Brundish, Derek Edward; Rink, Hans; Gruetter, Markus; Priestle, John Peter; Schmitz, Albert

PATENT ASSIGNEE(S): Ciba-Geigy A.-g., Switz.; UCP GEN-Pharma AG

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

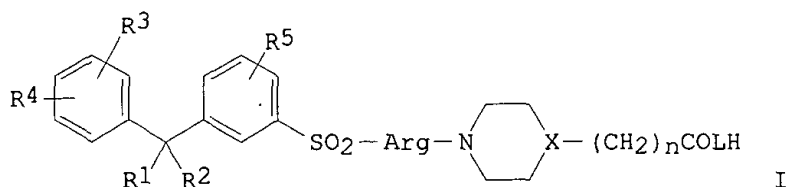
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 9322344 | A1 | 19931111 | WO 1993-EP908 | 19930415 |
| W: AU, CA, JP, KR, NZ, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9339533 | A1 | 19931129 | AU 1993-39533 | 19930415 |
| AU 674513 | B2 | 19970102 | | |
| EP 637318 | A1 | 19950208 | EP 1993-908944 | 19930415 |
| EP 637318 | B1 | 19980401 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 07505896 | T2 | 19950629 | JP 1993-518866 | 19930415 |
| AT 164595 | E | 19980415 | AT 1993-908944 | 19930415 |
| ZA 9302876 | A | 19941019 | ZA 1993-2876 | 19930423 |
| US 5686564 | A | 19971111 | US 1994-325253 | 19941020 |
| PRIORITY APPLN. INFO.: | | | GB 1992-9032 | 19920425 |
| | | | WO 1993-EP908 | 19930415 |
| OTHER SOURCE(S): | | | MARPAT 121:73891 | |
| GI | | | | |



AB Novel compds. ((I) R1, R2 = H, C1-C4 alkyl or R1+R2 = C3-C7 cycloalkyl; R3, R4, R5 independently H, C1-C4 alkyl, OH, OR6, SR6, halogen, NR7R8, NO2, CN, CONR7R8 or CO2R9; R6 = C1-C4 alkyl or C7-C10 aralkyl and R7, R8 and R9 are independently H, C1-C4 alkyl or C7-C10 aralkyl or R7 + R8 and the N atom to which they are bound form 5 or 6 membered azacycloalkyl or oxazacycloalkyl; Arg = arginine; X = CH, N; n is an integer from 0 to 7; L is a peptide linker, and H is the carboxy terminal end of hirudin), or their salts are useful for the treatment or prevention of thrombosis or diseases caused by thrombosis or for the detn. of thrombin in blood as diagnostic reagents. The C-terminal decapeptide of hirudin was synthesized as a resin bound, protected peptide with an N-terminal extension of GGGGN by Fmoc chem. T-butoxycarbonyl Arg(NO2)-OH 11.7 g in DMF 60 mL was incubated with N-Me morpholine 4.04 mL and iso-Bu chloroformate 4.8 mL at -10.degree. and mixed with an equal vol. of DMF contg. N-Me morpholine 4.04 mL and 4-(2-carboxyethyl)piperidine Me ester acetate salt 8.5 g to give 1-((S)-N.alpha.-t-butyloxycarbonyl-N.omega.-nitroarginyl)-4-(2-carboxyethyl)piperidine Me ester. The t-butyloxycarbonyl was cleaved to give 1-((S)-N.omega.-nitroarginyl)-4-(2-carboxyethyl)piperidine Me ester hydrochloride that was then conjugated with 3-(.alpha.,.alpha.-dimethylbenzyl) benzenesulfonyl chloride to give 1-(N.alpha.-3-(.alpha.,.alpha.-dimethylbenzyl)benzenesulfonyl-(S)-arginyl)-4-(2-carboxyethyl)-piperidine Me ester acetate salt. The ester was then hydrolyzed to give the hydrochloride: 1-(N.alpha.-3-(.alpha.,.alpha.-dimethylbenzyl)benzenesulfonyl-(S)-arginyl)-4-(2-carboxyethyl)-piperidine hydrochloride (II). The free base of II was then incubated with the protected hirudin peptide in the presence of TBTU and diisopropylethylamine followed by acid cleavage of the conjugate from the carrier and deprotection.

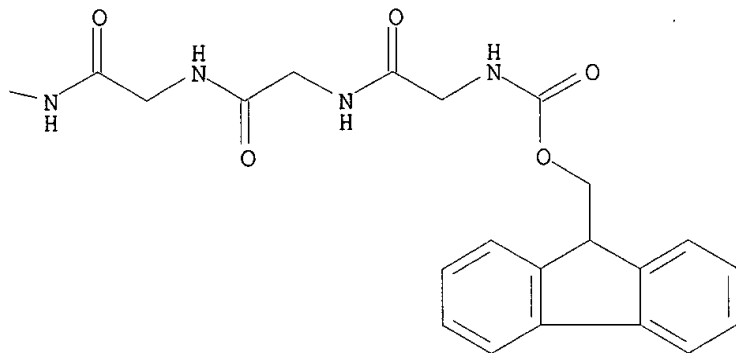
IT 154938-66-6DP, resin conjugates 154971-80-9DP, resin conjugates

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reactions of, in prepn. dimethylbenzenesulfonyl arginyl piperidine derivs. of hirudin for use as antithrombotics)

RN 154938-66-6 HCAPLUS

CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycylglycylglycyl-N-(triphenylmethyl)-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-O-(1,1-dimethylethyl)-L-tyrosyl-, 7,9,10,13,14-pentakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

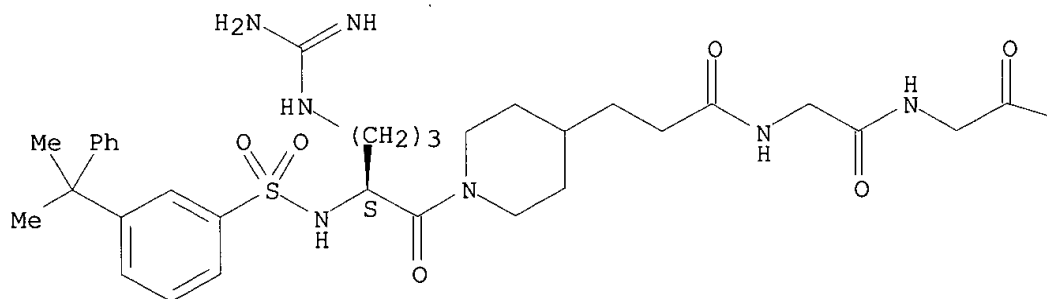
Absolute stereochemistry.



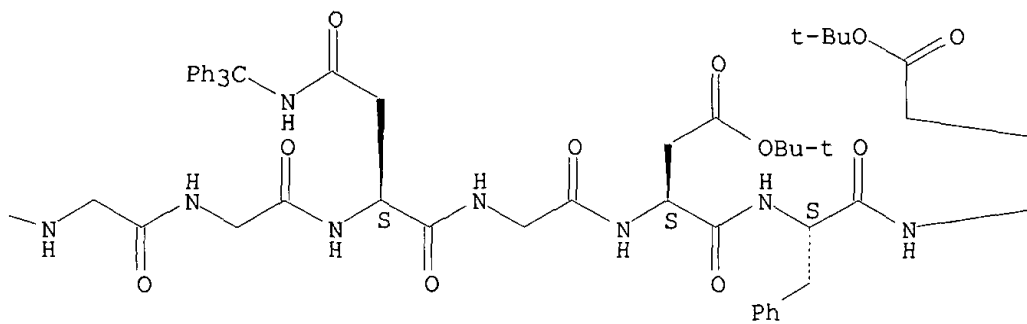
RN 154971-80-9 HCAPLUS

CN L-Leucine, N-{3-[1-[5-[(aminoiminomethyl)amino]-2-[[[3-(1-methyl-1-phenylethyl)phenyl]sulfonyl]amino]-1-oxopentyl]-4-piperidinyl]-1-oxopropyl]glycylglycylglycylglycyl-N-(triphenylmethyl)-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-O-(1,1-dimethylethyl)-L-tyrosyl-, 7,9,10,13,14-pentakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

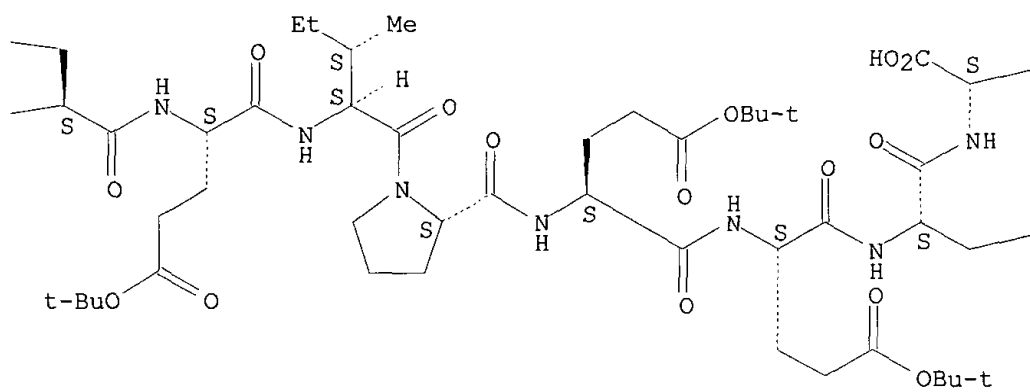
Absolute stereochemistry.



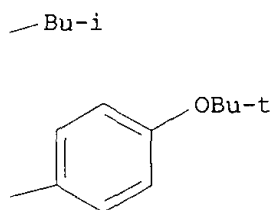
PAGE 1-B



PAGE 1-C

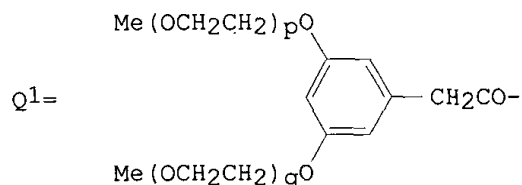
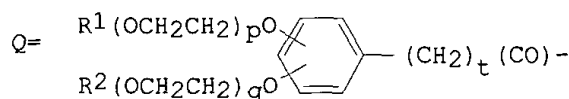


PAGE 1-D



L24 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:55012 HCAPLUS
 DOCUMENT NUMBER: 120:55012
 TITLE: Preparation of peptide with cell adhesion activity and
 polymeric modification thereof
 INVENTOR(S): Azuma, Ichiro; Saiki, Ikuo; Kusunose, Naoto; Ikeda,
 Yoshiharu; Ono, Keiichi
 PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

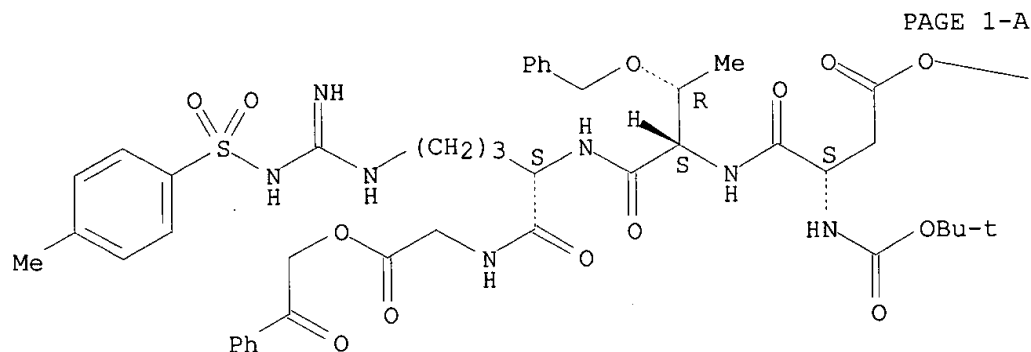
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|------------------|-----------------|------------|
| WO 9312140 | A1 | 19930624 | WO 1992-JP1594 | 19921207 |
| W: CA, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| JP 05170796 | A2 | 19930709 | JP 1991-355319 | 19911219 |
| JP 3235855 | B2 | 20011204 | | |
| PRIORITY APPLN. INFO.: | | | JP 1991-355319 | A 19911219 |
| OTHER SOURCE(S): | | MARPAT 120:55012 | | |
| GI | | | | |



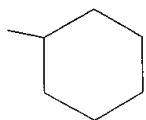
AB R-(Arg-Gly-Asp-Thr)_n-OH [I; n = 5-20; R = H, polyethylene glycol Q or R³(OCH₂CH₂)_kO(CO)(CH₂)_u(CO); wherein R¹, R², R³ = lower alkyl; k, p, q = any pos. integer to make the av.-mol.-wt. of the polyethylene glycol portion .apprx.1,000 to .apprx.12,000; t, u = 0, any pos. integer], useful as cancer metastasis, blood platelet aggregation, and bone absorption inhibitors, are prep'd. Thus, condensation of Boc-Arg(Tos)-Gly-[Asp(OcHex)-Thr(Bzl)-Arg(Tos)-Gly]₄-OH (Tos = p-MeC₆H₄SO₂, cHex = cyclohexyl, Bzl = CH₂Ph) (prepn. given) with H-[Asp(OcHex)-Thr(Bzl)-Arg(Tos)-Gly]₆-Asp(OcHex)-Thr(Bzl)-OBzl (prepn. given) in the presence of 1-ethyl-2-(3-diethylaminopropyl)carbodiimide hydrochloride and 1-hydroxybenzotriazole in DMF and N-methylpyrrolidinone at 5-10.degree. followed by deprotection with HF in anisole and MeSSEt and purifn. using reversed phase HPLC gave I (n = 11, R = H) (II). N-acylation of II with hydrocinnamic acid deriv. Q¹-OSu (Su = N-succinimidyl) (av.-mol.-wt. .apprx.10,000) in 0.1M borate buffer at room temp. gave, after purifn. using reversed phase HPLC, a II-polyethylene glycol conjugate I (n = 11, R = Q¹) (III). II at 500 .mu.g and III at 40-1,000 .mu.g inhibited the metastasis of B16-BL6 melanoma cells to lungs in mice. Also prep'd. were I

(n = 1,3,5,7,9) and 5 polyethylene glycol conjugates .
 IT 152016-42-7 152016-43-8
 RL: RCT (Reactant)
 (peptide coupling of, in prepn. of peptides and their
 conjugates with polyethylene glycols with cell adhesion
 activity)
 RN 152016-42-7 HCAPLUS
 CN Glycine, N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl]-O-(
 phenylmethyl)-L-threonyl]-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methy
 l]-L-ornithyl]-, 4-cyclohexyl 1-(2-oxo-2-phenylethyl) ester (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

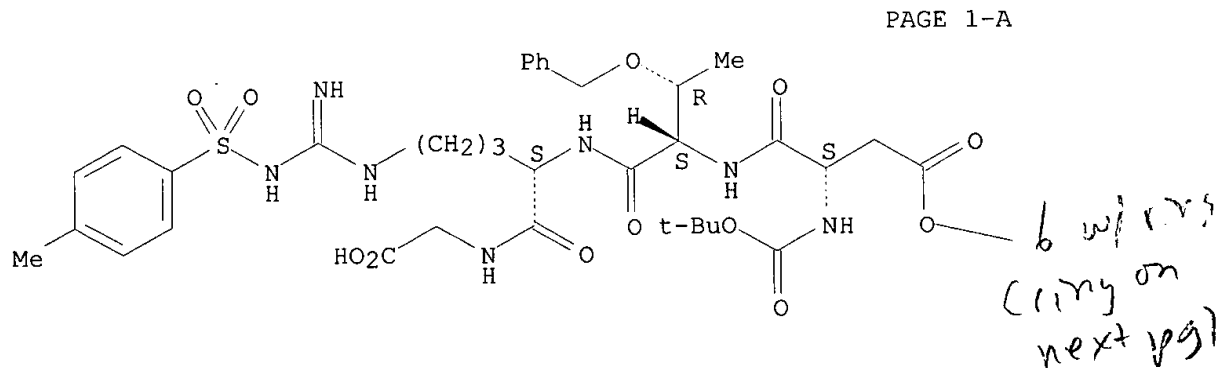


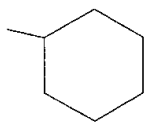
PAGE 1-B



RN 152016-43-8 HCAPLUS
 CN Glycine, N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-.alpha.-aspartyl]-O-(
 phenylmethyl)-L-threonyl]-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methy
 l]-L-ornithyl]-, 4-cyclohexyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L24 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:586825 HCAPLUS

DOCUMENT NUMBER: 113:186825

TITLE: Synthetic peptide mimics of the active domain of fibronectin

AUTHOR(S): Davies, John S.; Orchison, Jack J. A.; Jones, Gareth E.

CORPORATE SOURCE: Dep. Chem., Univ. Coll. Swansea, London, UK

SOURCE: Biochem. Soc. Trans. (1990), 18(6), 1326-8

CODEN: BCSTB5; ISSN: 0300-5127

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the study of cell-adhesion and cell-spreading properties of fibronectin and the properties of focal domain sequence Arg-Gly-Asp-Ser, the model peptide cyclo-(Asp-Ser-Lys-Arg-Gly) was prepd. and studied. Other analogs were also examd. for their effect on cell adhesion and spreading. The role of conformation in these processes was examd.

IT **130126-33-9D**, pepsyn K **conjugates**

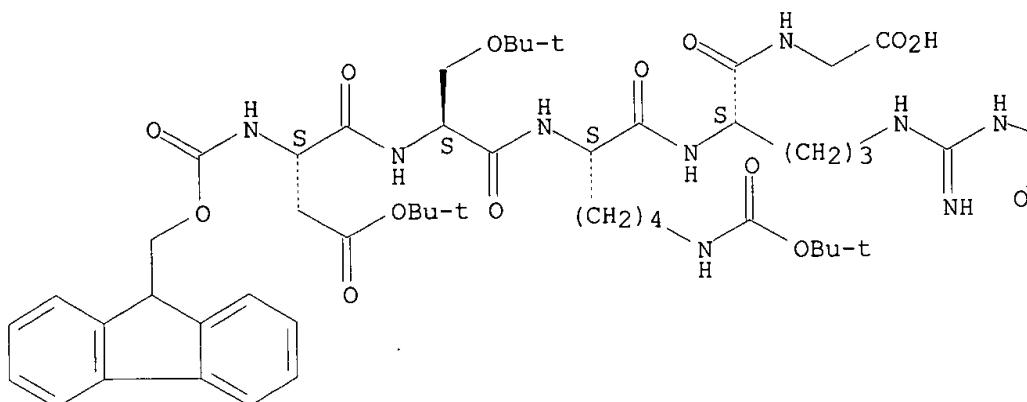
RL: RCT (Reactant)
(hydrolysis of)

RN 130126-33-9 HCAPLUS

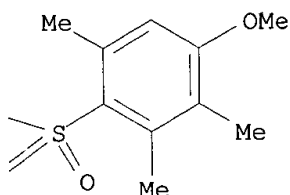
CN Glycine, N-[N2-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-[O-(1,1-dimethylethyl)-N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-.alpha.-aspartyl]-L-seryl]-L-lysyl]-N5-[imino[[4-methoxy-2,3,6-trimethylphenyl)sulfonyl]amino]methyl]-L-ornithyl]-, 4-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1989:33729 HCAPLUS
 DOCUMENT NUMBER: 110:33729
 TITLE: Preparation of antibody conjugates of amine derivatives of folic acid analogs for treatment of cellular disorders
 INVENTOR(S): Coughlin, Daniel J.; Radcliffe, Robert D.; Lopes, Anthony Dwight; Rodwell, John D.
 PATENT ASSIGNEE(S): Cytogen Corp., USA
 SOURCE: PCT Int. Appl., 60 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 8706837 | A1 | 19871119 | WO 1987-US992 | 19870501 |
| W: AU, BR, DK, FI, JP | | | | |
| CA 1330378 | A1 | 19940621 | CA 1987-536091 | 19870430 |
| AU 8773590 | A1 | 19871201 | AU 1987-73590 | 19870501 |
| JP 63503144 | T2 | 19881117 | JP 1987-502915 | 19870501 |
| JP 2564586 | B2 | 19961218 | | |
| EP 251455 | A2 | 19880107 | EP 1987-304093 | 19870507 |
| EP 251455 | A3 | 19900905 | | |
| EP 251455 | B1 | 19940511 | | |
| R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE | | | | |

| | | | | |
|------------|----|----------|----------------|----------|
| AT 105484 | E | 19940515 | AT 1987-304093 | 19870507 |
| ES 2051738 | T3 | 19940701 | ES 1987-304093 | 19870507 |
| ZA 8703305 | A | 19880127 | ZA 1987-3305 | 19870508 |
| FI 8800059 | A | 19880107 | FI 1988-59 | 19880107 |
| DK 8800051 | A | 19880415 | DK 1988-51 | 19880107 |
| US 5140104 | A | 19920818 | US 1989-426374 | 19891024 |

PRIORITY APPLN. INFO.:

| | |
|----------------|----------|
| US 1986-861037 | 19860508 |
| US 1982-356315 | 19820309 |
| US 1984-646327 | 19840831 |
| US 1984-646328 | 19840831 |
| US 1984-650375 | 19840913 |
| US 1984-650754 | 19840913 |
| WO 1987-US992 | 19870501 |
| EP 1987-304093 | 19870507 |

AB Therapeutic antibody conjugates comprise amine derivs. of folic acid analogs covalently attached via a reactive amine group to an oxidized carbohydrate moiety of an antibody or antibody fragment. The oligosaccharide moiety of a rat monoclonal antibody specific for a class I major histocompatibility antigen was oxidized by incubation in the dark on ice with a NaIO₄ soln. pH 6.0 for 1. The modified antibody was then coupled to methotrexate- γ -hydrazide (prepd. by, e.g. the mixed anhydride method from 4-amino-4-deoxy-N¹⁰-Me pteronic acid and L-glutamic acid α -tert-Bu ester- γ -N'-butoxycarbonyl hydrazide) by incubation in the dark at room temp. overnight. In vivo therapeutic effect of the conjugate was tested on BN tumor-bearing nude mice by i.p. injection. Animals receiving the conjugate underwent tumor regression. Animals treated with antibodies having randomly attached methotrexate- γ -hydrazide only showed a slight therapeutic effect.

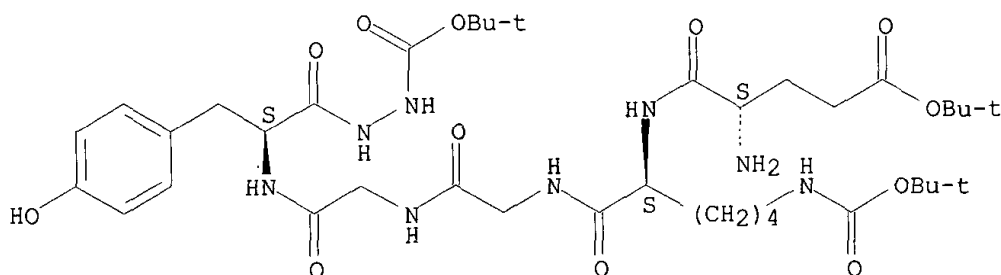
IT 118359-49-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in prepn. of folic acid analog for **conjugation**
with antibodies)

RN 118359-49-2 HCAPLUS

CN L-Tyrosine, N-[N-[N-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-L- α -glutamyl-L-lysyl]glycyl]glycyl]-, 5-(1,1-dimethylethyl) ester, 1-[2-[(1,1-dimethylethoxy)carbonyl]hydrazide] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1978:444196 HCAPLUS

DOCUMENT NUMBER: 89:44196

TITLE: Synthesis of hapten-polypeptide conjugates as antigen models for the N-terminal region of the α -2-chain of rabbit skin collagen

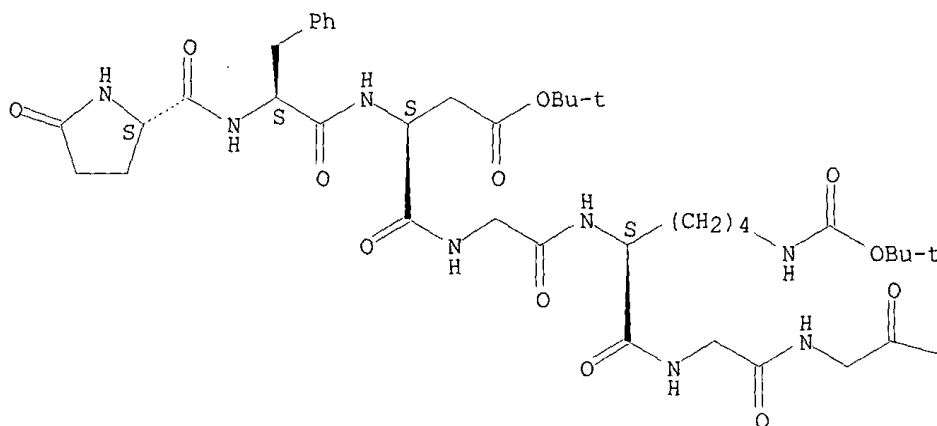
AUTHOR(S): Nokiara, Kiyoshi; Berndt, Heinz

CORPORATE SOURCE: Deutsches Wollforschungsinstitut, Tech. Hochsch.,

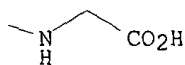
Aachen, Ger.
 SOURCE: J. Chem. Soc., Perkin Trans. 1 (1978), (3), 260-3
 CODEN: JCPRB4; ISSN: 0300-922X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB H-pyroGlu-Phe-Asp-Gly-Lys-Gly-Gly-Gly-OH was prepd. as the antigenic determinant representing the .alpha.-2-chain of rabbit skin collagen. H-pyroGlu-Phe-Asp(OCMe₃)-Gly-Lys(CO₂CMe₃)-Gly-Gly-Gly-OH was conjugated to the carriers multichain .epsilon.-poly-DL-Ala-L-Lys and copoly(Tyr-Lys) ; the latter conjugates can be used for immunological studies.
 IT **66789-43-3P**
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and **conjugation** of, with polypeptides)
 RN 66789-43-3 HCAPLUS
 CN Glycine, N-[N-[N-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-[N-[N-[N-(5-oxo-L-prolyl)-L-phenylalanyl]-L-.alpha.-aspartyl]glycyl]-L-lysyl]glycyl]glycyl]-, 4-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CANELLA 09/544,644

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 L4 9059 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

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L14 SCREEN 1993 AND 2005

L15 SCREEN 2127

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L17 414451 S L13 AND SQL<20

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L19 0 S L10 SSS SAM SUB=L17

L20 224 S L10 SSS FUL SUB=L17

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L22 85 S L20

L23 103 S L21-22

L24 41 S L23 AND PATENT/DT

L25 33 S L24 AND PRD<19990704

L26 2 S L25 AND ?CONJUGAT? 2 cites

L27 31 S L25 NOT L26

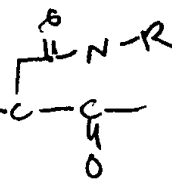
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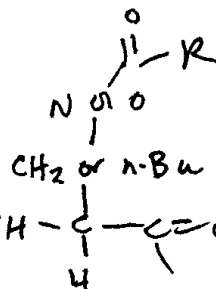
L30 2 S L29 AND (HYDROPHOB? OR LIPOPHIL?) 2 cites

L31 28 S L29 NOT L30

remaining cites for L29



25 peptide w/



224 peptide w/

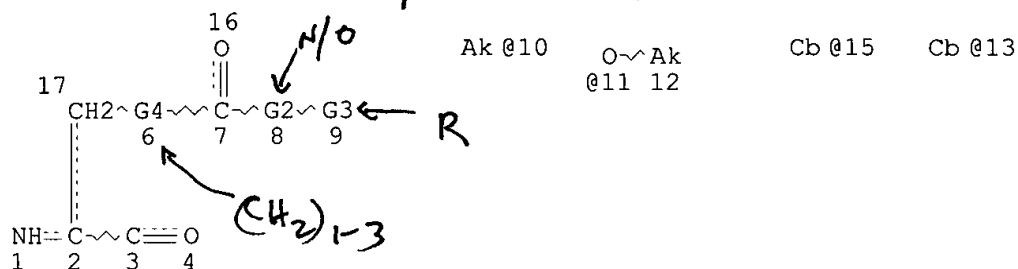
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parent STR



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CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 12
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY SAT AT 13
GGCAT IS MCY UNS AT 15
DEFAULT ECLEVEL IS LIMITED
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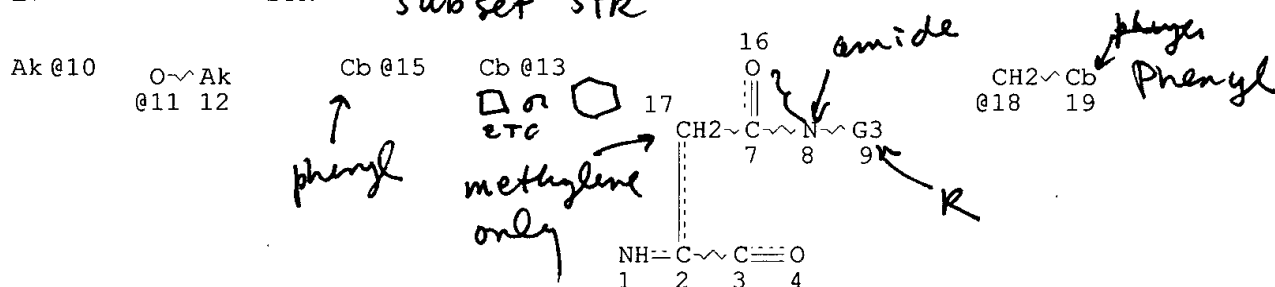
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NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

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L7 STR *subset 50*

subset STR



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CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 12
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY SAT AT 13
GGCAT IS MCY UNS AT 15
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DEFAULT ECLEVEL IS LIMITED
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ECOUNT IS M2 C AT 12
ECOUNT IS X6 C AT 13
ECOUNT IS E6 C AT 15
ECOUNT IS E6 C AT 19

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L9 25 SEA FILE=REGISTRY SUB=L4 SSS FUL L7
L21 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L9

=> d que 122

L10

STR

Ak @10

O~Ak
@11 12

Cb @15

*saturated
carbocyclic*

Cb @13

o/n

16

17

G2

G1

C

G3

6

7

9

*R**n-butyl*NH~C~C~O
1 2 3 4CH2~Cb
@18 19

VAR G1=NH/O
 VAR G2=CH2/N-BU
 VAR G3=10/11/13/15/18
 NODE ATTRIBUTES:
 CONNECT IS E3 RC AT 2
 CONNECT IS E1 RC AT 10
 CONNECT IS E1 RC AT 12
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 GGCAT IS MCY SAT AT 13
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GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L11 710561 SEA FILE=REGISTRY ABB=ON PLU=ON PROTEIN/FS AND SQL<101
 L13 686268 SEA FILE=REGISTRY ABB=ON PLU=ON L11 AND NC=1
 L17 414451 SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND SQL<20
 L20 224 SEA FILE=REGISTRY SUB=L17 SSS FUL L10
 L22 85 SEA FILE=HCAPLUS ABB=ON PLU=ON L20

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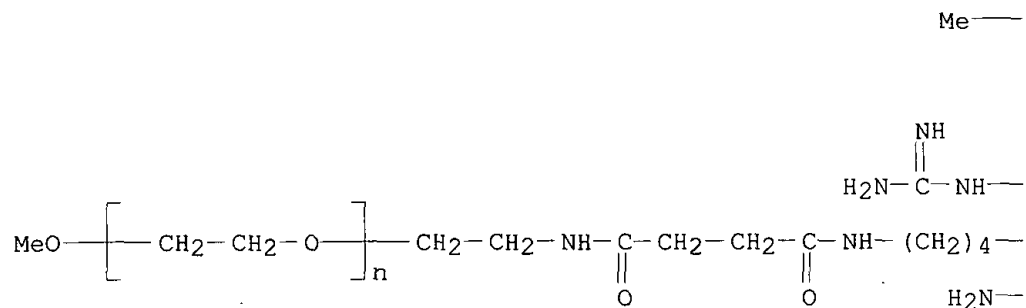
CANELLA 09/544,644

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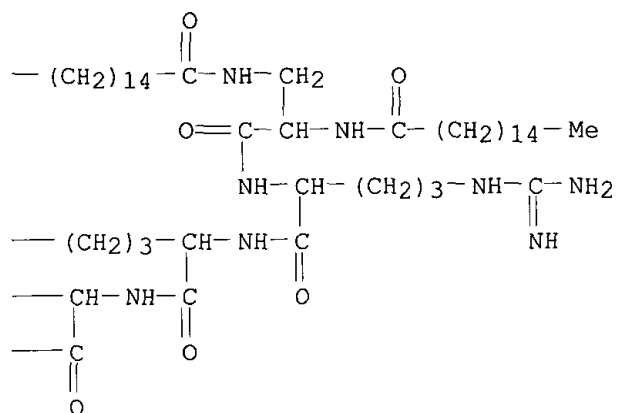
L26 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:708651 HCAPLUS
 DOCUMENT NUMBER: 131:319900
 TITLE: Diagnostic/therapeutic agents comprising
 membrane-forming amphiphilic lipopeptide-stabilized
 gas microbubbles
 INVENTOR(S): Cuthbertson, Alan; Solbakken, Magne; Wolfe, Henry
 Raphael
 PATENT ASSIGNEE(S): Marsden, John Christopher, UK; Nycomed Imaging A/S
 SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|---|----------|-----------------|--------------|
| WO 9955383 | A2 | 19991104 | WO 1999-GB1247 | 19990422 <-- |
| WO 9955383 | A3 | 20000706 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2329778 | AA | 19991104 | CA 1999-2329778 | 19990422 <-- |
| EP 1073475 | A2 | 20010207 | EP 1999-918154 | 19990422 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AU 9936187 | A1 | 19991116 | AU 1999-36187 | 19990423 <-- |
| NO 2000005382 | A | 20001218 | NO 2000-5382 | 20001026 <-- |
| PRIORITY APPLN. INFO.: GB 1998-9084 A 19980428 <-- | | | | |
| WO 1999-GB1247 W 19990422 <-- | | | | |
| AB | Novel membrane-forming amphiphilic lipopeptides comprise one or more peptide moieties contg. 2-50 aminoacyl residues and one or more hydrocarbon chains contg. 5-50 carbon atoms. Such lipopeptides may be used in the formation of stabilized gas microbubble dispersions suitable for use as diagnostic and/or therapeutic agents, for example as ultrasound contrast agents. Perfluorobutane-contg. microbubbles were prepd. that used N-[3-(2-aminoethanamido)-5-[2-(n-hexadecyl)octadecanamido]benzoyl]gly cine (prepn. given) as the membrane-forming agent. | | | |
| IT | 248602-48-4P RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses) (diagnostic/therapeutic agents comprising membrane-forming amphiphilic lipopeptide-stabilized gas microbubbles) | | | |
| RN | 248602-48-4 HCAPLUS | | | |
| CN | Poly(oxy-1,2-ethanediyl), .alpha.-methoxy-.omega.-hydroxy-, ether with N-(1-oxohexadecyl)-3-[(1-oxohexadecyl)amino]-L-alanyl-L-arginyl-L-arginyl- N6-[4-[(2-hydroxyethyl)amino]-1,4-dioxobutyl]-L-lysineamide (9CI) (CA INDEX NAME) | | | |

PAGE 1-A



PAGE 1-B



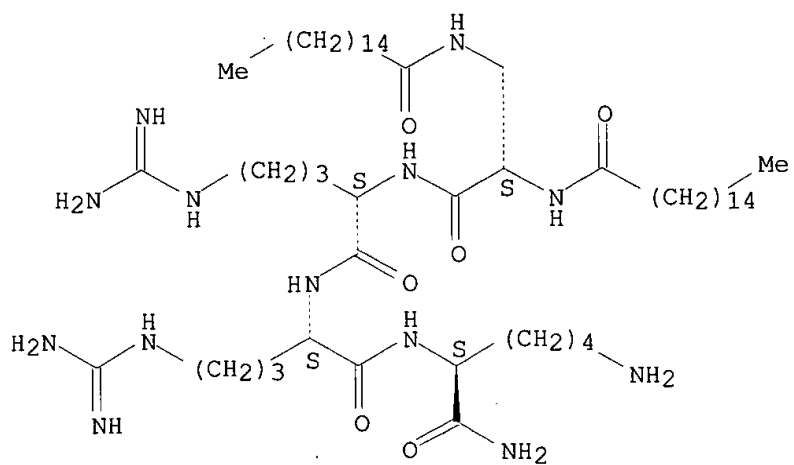
IT 247231-44-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(diagnostic/therapeutic agents comprising membrane-forming amphiphilic
lipopeptide-stabilized gas microbubbles)

RN 247231-44-3 HCAPLUS

CN L-Lysinamide, N-(1-oxohexadecyl)-3-[(1-oxohexadecyl)amino]-L-alanyl-L-
arginylyl-L-arginylyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 2

L26 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:440179 HCAPLUS

DOCUMENT NUMBER: 127:51009

TITLE: Peptide **conjugates** derived from thymic hormones and their compositions for use as drugs

INVENTOR(S): Dussourd, D'hinterland Lucien; Pinel, Anne-Marie

PATENT ASSIGNEE(S): Societe D'etude Et De Recherche De Pathologie Appliquee - Serpa, Fr.; Dussourd D'hinterland, Lucien; Pinel, Anne-Marie

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 9718239 | A1 | 19970522 | WO 1996-FR1812 | 19961115 <-- |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| FR 2741076 | A1 | 19970516 | FR 1995-13544 | 19951115 |
| FR 2741076 | B1 | 19980130 | | |
| CA 2237995 | AA | 19970522 | CA 1996-2237995 | 19961115 <-- |
| AU 9676832 | A1 | 19970605 | AU 1996-76832 | 19961115 <-- |
| EP 861266 | A1 | 19980902 | EP 1996-939132 | 19961115 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000500447 | T2 | 20000118 | JP 1997-518639 | 19961115 <-- |
| US 6211155 | B1 | 20010403 | US 1998-68767 | 19980824 <-- |
| PRIORITY APPLN. INFO.: | | | FR 1995-13544 | A 19951115 <-- |
| | | | WO 1996-FR1812 | W 19961115 <-- |

OTHER SOURCE(S): MARPAT 127:51009

AB Peptide **conjugates** have been synthesized which have a sequence of at least 3 amino acids derived from a thymic hormone selected from thymuline and thymopoietine (the amino acids are in the D, L, or DL form) and in which the sequence is **conjugated** to a mono- or dicarboxylic acid. The peptide **conjugates** are used in pharmaceutical or cosmetic compns. Thus, Ac-Pyro-Ala-Lys-Ser-Gln-Gly-Gly-Ser-Asn-NH₂ was prepd. and tested in regards to cellular activity.

IT **191221-06-4P**

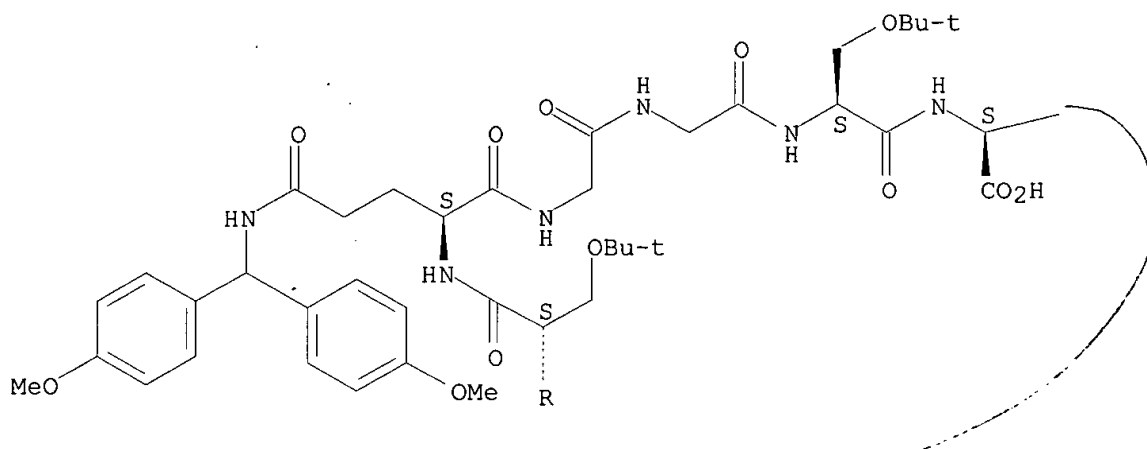
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(peptide **conjugates** derived from thymic hormones and their compns. for use as drugs)

RN 191221-06-4 HCAPLUS

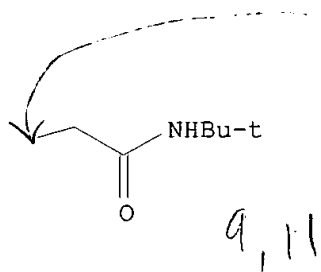
CN 2-9-Thymulin (swine peptide moiety), 3-[N⁶-[(1,1-dimethylethoxy)carbonyl]-L-lysine]-4-[O-(1,1-dimethylethyl)-L-serine]-5-[N-[bis(4-methoxyphenyl)methyl]-L-glutamine]-8-[O-(1,1-dimethylethyl)-L-serine]-9-[N-(1,1-dimethylethyl)-L-asparagine]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

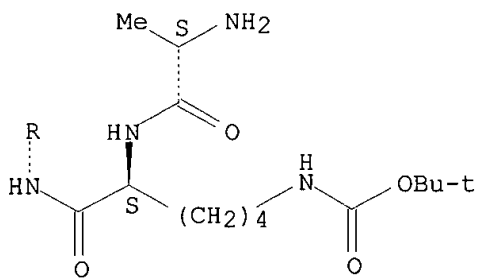
PAGE 1-A



PAGE 1-B



PAGE 2-A



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L28 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:958268 HCAPLUS
 DOCUMENT NUMBER: 123:350253
 TITLE: Aerosol drug formulations containing vitamin E
 INVENTOR(S): Fu, Lu Mou-ying; Gupta, Pramod K.; Adjei, Akwete L.
 PATENT ASSIGNEE(S): Abbott Laboratories, USA
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 9524892 | A1 | 19950921 | WO 1995-US2764 | 19950302 <-- |
| W: AU, CA, JP, KR, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9519804 | A1 | 19951003 | AU 1995-19804 | 19950302 <-- |
| AU 709783 | B2 | 19990909 | | |
| JP 09510445 | T2 | 19971021 | JP 1995-524061 | 19950302 <-- |
| EP 804157 | A1 | 19971105 | EP 1995-912746 | 19950302 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| PRIORITY APPLN. INFO.: | | | US 1994-212472 | 19940314 <-- |
| | | | WO 1995-US2764 | 19950302 <-- |

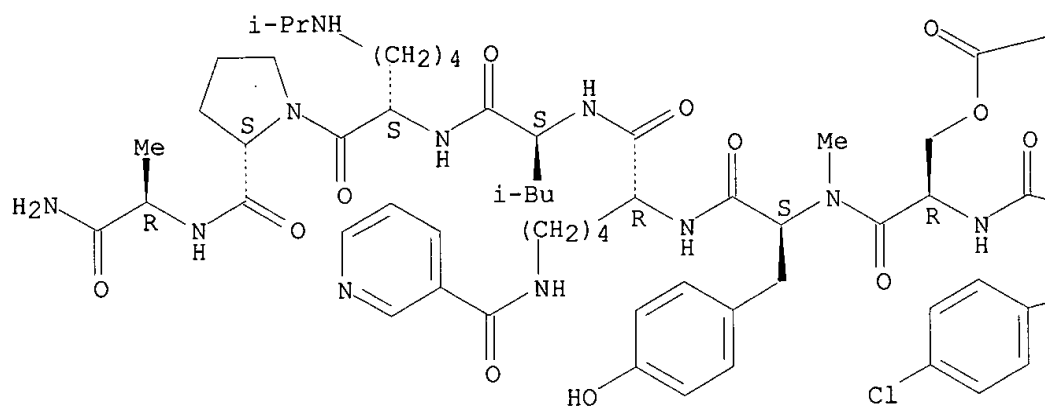
AB Pharmaceutical compns. for aerosol **delivery** are disclosed comprising (a) a medicament, (b) a non-chlorofluorocarbon propellant, and (c) tocopherol or a pharmaceutically acceptable deriv. thereof, as well as a method for prepg. such compns. in which unwanted aggregation of the medicament is prevented without the use of surfactants or cosolvents. Pharmaceutical aerosols contg. leuprolide acetate in 0.1% d-.alpha. tocopheryl acetate (I) and 10mL HFC-134a were prepd. having good dispersion quality as compared with controls without I which had poor dispersion quality.

IT **170929-31-4**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aerosol drug formulations contg. vitamin E)

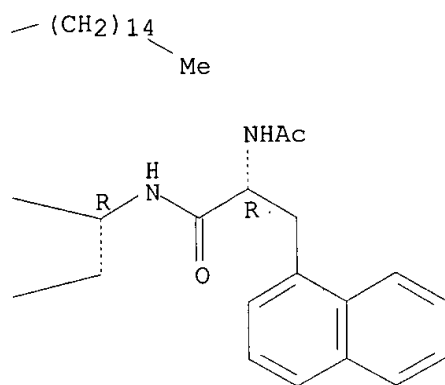
RN 170929-31-4 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(1-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-O-(1-oxohexadecyl)-D-seryl-N-methyl-L-tyrosyl-N6-(3-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2

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L30 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:690991 HCAPLUS
DOCUMENT NUMBER: 131:308623
TITLE: Ultrasound imaging contrast agents, particularly for perfusion in the myocardium
INVENTOR(S): Eriksen, Morten; Tolleshaug, Helge; Skurtveit, Roald; Cuthbertson, Alan; Ostensen, Jonny; Frigstad, Sigmund; Rongved, Pal
PATENT ASSIGNEE(S): Marsden, John Christopher, UK; Nycomed Imaging AS
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

*Search # 2
covers species
1-3, 7, 9, 11*

| PATENT NO. | KIND | DATE | DATE |
|--|------|----------|---|
| WO 9953963 | A1 | 1999102 | 19990422 <-- |
| W: AE, AL, AM, AT, AU, CZ, DE, DK, HR, HU, ID, IL, IN, IS, LT, LU, LV, MD, MG, MK, SE, SG, SI, SK, SL, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | CA, CH, CN, CU, GD, GE, GH, GM, LC, LK, LR, LS, PT, RO, RU, SD, US, UZ, VN, YU, |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2329175 | AA | 19991028 | CA 1999-2329175 19990422 <-- |
| AU 9936172 | A1 | 19991108 | AU 1999-36172 19990422 <-- |
| BR 9909822 | A | 20001219 | BR 1999-9822 19990422 <-- |
| EP 1073473 | A1 | 20010207 | EP 1999-918133 19990422 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| NO 2000005250 | A | 20001218 | NO 2000-5250 20001019 <-- |
| PRIORITY APPLN. INFO.: | | | GB 1998-8599 A 19980422 <-- US 1998-84880P P 19980508 <-- WO 1999-GB1221 W 19990422 <-- |

AB Ultrasonic visualization of a subject, particularly of perfusion in the myocardium and other tissues, is performed using novel gas-contg. contrast agent preps. which promote controllable and temporary growth of the gas phase in vivo following administration and can therefore act as deposited perfusion tracers. The preps. comprise an injectable aq. medium comprising dispersed gas and an injectable oil-in-water emulsion in which the oil phase comprises a diffusible component capable of diffusion in vivo into the dispersed gas to promote temporary growth thereof, such that material present at the surfaces of the dispersed gas phase and material present at the surfaces of the dispersed oil phase have affinity for each other, e.g. as a result of having opposite charges. In cardiac perfusion imaging the preps. may advantageously be coadministered with vasodilator drugs such as adenosine in order to enhance the differences between return signal intensity from normal and hypoperfused myocardial tissue resp. A neg.-charged perfluorobutane gas dispersion and a pos.-charged perfluorodimethylcyclobutane emulsion were simultaneously injected i.v. into a dog. The resulting myocardial contrast effect was far more intense than that obsd. when the dispersion and emulsion were both neg.-charged. The contrast lasted for 20 min.

IT 247231-44-3P

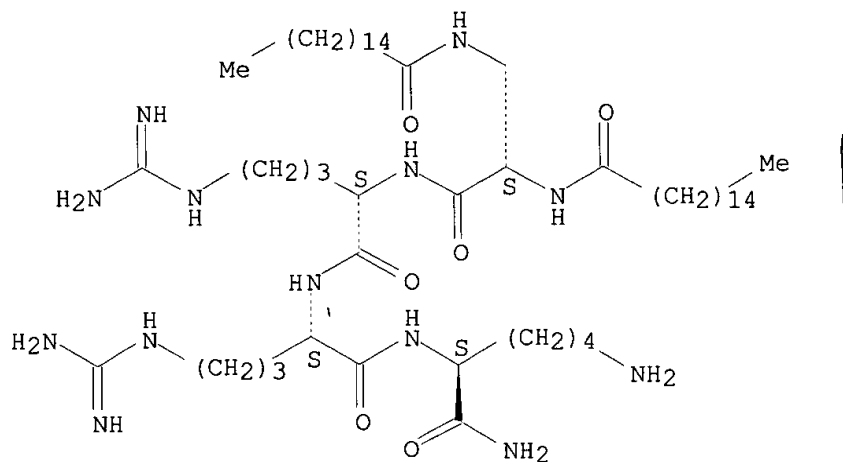
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ultrasound imaging contrast agents, particularly for perfusion in the myocardium)

RN 247231-44-3 HCAPLUS

CN L-Lysinamide, N-(1-oxohexadecyl)-3-[(1-oxohexadecyl)amino]-L-alanyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

14

THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L30 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:731839 HCAPLUS

DOCUMENT NUMBER: 126:8711

TITLE: Preparation of bicyclic peptide tachykinin NK2 antagonists.

INVENTOR(S): Arcamone, Federico; Maggi, Carlo Alberto; Quartara, Laura; Giannotti, Danilo

PATENT ASSIGNEE(S): A. Menarini Industrie Farmaceutiche Riunite S.R.L., Italy

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

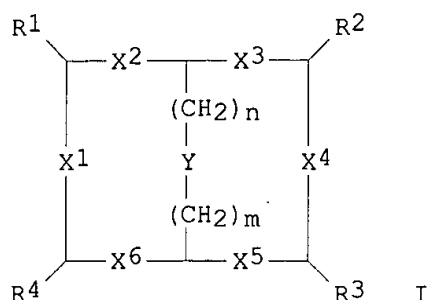
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|-----------------|----------|-----------------|----------------|
| WO 9628467 | A1 | 19960919 | WO 1996-EP1028 | 19960311 <-- |
| W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| IL 117395 | A1 | 19991231 | IL 1996-117395 | 19960307 <-- |
| CA 2215372 | AA | 19960919 | CA 1996-2215372 | 19960311 <-- |
| AU 9651059 | A1 | 19961002 | AU 1996-51059 | 19960311 <-- |
| AU 696528 | B2 | 19980910 | | |
| BR 9607348 | A | 19971230 | BR 1996-7348 | 19960311 <-- |
| EP 815126 | A1 | 19980107 | EP 1996-907421 | 19960311 <-- |
| EP 815126 | B1 | 20010103 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| CN 1183786 | A | 19980603 | CN 1996-193762 | 19960311 <-- |
| JP 11501643 | T2 | 19990209 | JP 1996-527267 | 19960311 <-- |
| CZ 287372 | B6 | 20001115 | CZ 1997-2862 | 19960311 <-- |
| AT 198481 | E | 20010115 | AT 1996-907421 | 19960311 <-- |
| ES 2155187 | T3 | 20010501 | ES 1996-907421 | 19960311 <-- |
| SK 281899 | B6 | 20010911 | SK 1997-1212 | 19960311 <-- |
| ZA 9601983 | A | 19970929 | ZA 1996-1983 | 19960312 <-- |
| NO 9704057 | A | 19971107 | NO 1997-4057 | 19970903 <-- |
| US 6150325 | A | 20001121 | US 1997-929215 | 19970909 <-- |
| PRIORITY APPLN. INFO.: | | | IT 1995-FI44 | A 19950313 <-- |
| | | | WO 1996-EP1028 | W 19960311 <-- |
| OTHER SOURCE(S): | MARPAT 126:8711 | | | |
| GI | | | | |



AB Title compds. (I; X1-X6 = NRCO; R = H, alkyl; Y = NRCO, SS; .gtoreq.1 of R1-R4 = hydrophilic group, the others = **hydrophobic** groups; m, n = 1-4), were prepd. Thus, solid phase synthesis on chlorotrityl resin gave H-Asn[(Ac4O)-.beta.-D-Glc]-Asp(OtBu)-Trp-Phe-Dap(BOC)-Leu-OH (Glc = glucopyranosyl). The latter was cyclized using PyBOP/(Me2CH)2NEt to give 39% monocyclic product, which was deprotected with CF3CO2H and again cyclized with PyBOP/(Me2CH)2NEt followed by stirring with NaOMe in MeOH to give cyclo[[Asn(.beta.-D-Glc)-Asp-Trp-Phe-Dap-Leu]cyclo(2.beta.-5.beta.)] [I; X1-X6, Y = CONH; R1 = CH2CHMe2; R2 = CH2Ph; R3 = 3-indolylmethyl; R4 = CH2CONH-(.beta.-D-Glc); m, n = 1]. The latter at 10 nmol/kg i.v. in mice gave 50-70% inhibition of agonist-induced urinary bladder contractions.

IT 183747-30-0P 183747-32-2P

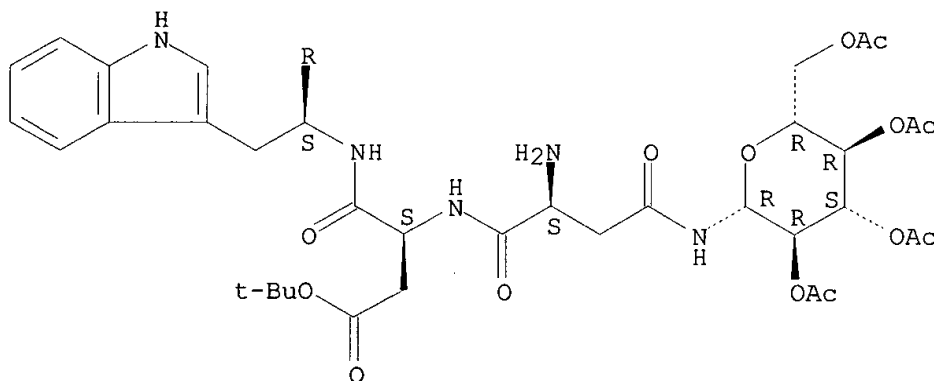
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bicyclic peptide tachykinin NK2 antagonists)

RN 183747-30-0 HCAPLUS

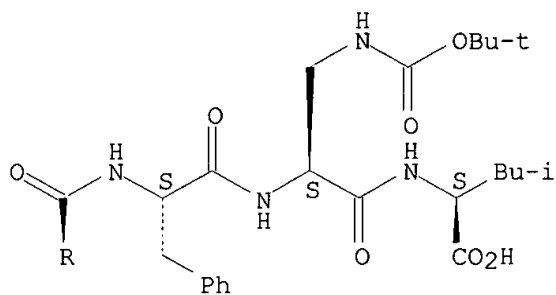
CN L-Leucine, N-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)-L-asparaginyl-L-.alpha.-aspartyl-L-tryptophyl-L-phenylalanyl-3-[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanyl-, 2-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

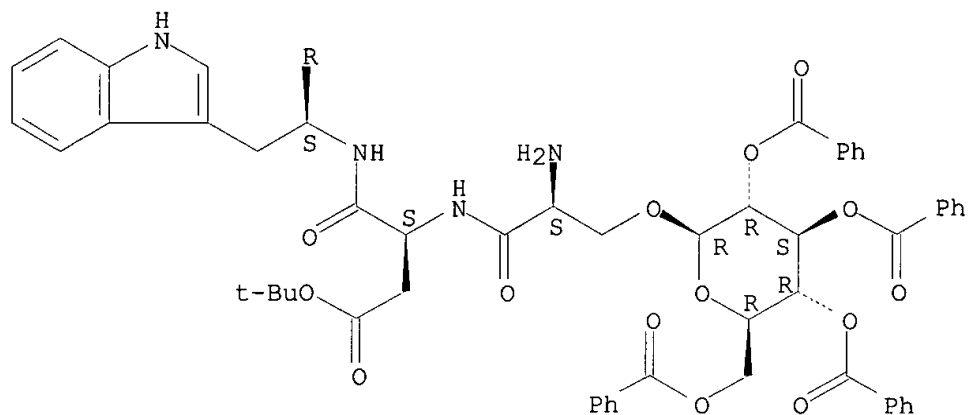


RN 183747-32-2 HCAPLUS

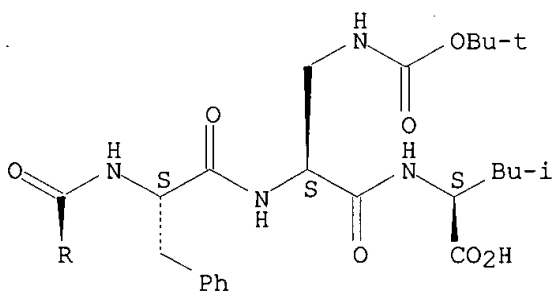
CN L-Leucine, O-(2,3,4,6-tetra-O-benzoyl-.beta.-D-glucopyranosyl)-L-seryl-L-.alpha.-aspartyl-L-tryptophyl-L-phenylalanyl-3-[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanyl-, 2-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



#2

CANELLA 09/544,644

only 1 patent per patent
family was displayed
in the full display to
save on display
cost

=> d t i p n 1-28

L31 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of luteinizing hormone releasing hormone analogs having a cytotoxic moiety

PATENT NO. KIND DATE

| | | | | |
|----|------------|----|----------|-----|
| PI | US 6214969 | B1 | 20010410 | <-- |
| | NO 9304541 | A | 19940207 | <-- |

L31 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of cyclopeptides or cyclic depsipeptides as antifungal agents

PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | JP 2000229998 | A2 | 20000822 | <-- |
|----|---------------|----|----------|-----|

L31 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of ring modified cyclic peptide analogs as antifungal agents

PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 2000011023 | A2 | 20000302 | <-- |
| | WO 2000011023 | A3 | 20000615 | |
| | AU 9955726 | A1 | 20000314 | <-- |
| | EP 1107981 | A2 | 20010620 | <-- |

L31 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Peptides, peptide analogs, peptidomimetics, and other small molecules useful for inhibiting the activity of ribonucleotide reductase

PATENT NO. KIND DATE

| | | | | |
|----|------------|---|----------|-----|
| PI | US 6030942 | A | 20000229 | <-- |
|----|------------|---|----------|-----|

L31 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of new antifungal agents, cyclic aeriothricin analogs, for treatment of infectious diseases caused by pathogenic microorganisms

PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 2000005251 | A1 | 20000203 | <-- |
| | AU 9951630 | A1 | 20000214 | <-- |
| | BR 9912367 | A | 20010502 | <-- |
| | EP 1100816 | A1 | 20010523 | <-- |

L31 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of peptides, peptidomimetics, and nonpeptides as medical and agrochemical antifungals.

PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 2000003743 | A2 | 20000127 | <-- |
| | WO 2000003743 | A3 | 20010201 | |
| | AU 9951075 | A1 | 20000207 | <-- |
| | EP 1096925 | A2 | 20010509 | <-- |

L31 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of novel cryptophycin pharmaceuticals

PATENT NO. KIND DATE

| | | | | |
|----|------------|----|----------|-----|
| PI | WO 9808505 | A1 | 19980305 | <-- |
| | AU 9741701 | A1 | 19980319 | <-- |
| | AU 722492 | B2 | 20000803 | |
| | EP 934065 | A1 | 19990811 | <-- |

| | | | | |
|--|------------|---|----------|-----|
| | BR 9711986 | A | 19990824 | <-- |
| | CN 1233957 | A | 19991103 | <-- |
| | NO 9900833 | A | 19990426 | <-- |

L31 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Preparation of heterocyclic peptide derivatives as farnesylprotein transferase inhibitors and anticancer agents
 PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 9745412 | A1 | 19971204 | <-- |
| | AU 9732151 | A1 | 19980105 | <-- |
| | EP 934270 | A1 | 19990811 | <-- |
| | JP 2000508335 | T2 | 20000704 | <-- |

L31 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Preparation of transferase inhibitors for treating cancer
 PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 9738664 | A2 | 19971023 | <-- |
| | WO 9738664 | A3 | 19971120 | |
| | CA 2251955 | AA | 19971023 | <-- |
| | AU 9728022 | A1 | 19971107 | <-- |
| | EP 952842 | A2 | 19991103 | <-- |
| | JP 2000513711 | T2 | 20001017 | <-- |

L31 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Preparation of imidazole derivatives and imidazole-contg. peptide analogs and a method of treating cancer
 PATENT NO. KIND DATE

| | | | | |
|----|---------------|----|----------|-----|
| PI | WO 9736587 | A1 | 19971009 | <-- |
| | CA 2250232 | AA | 19971009 | <-- |
| | AU 9727221 | A1 | 19971022 | <-- |
| | AU 727939 | B2 | 20010104 | |
| | EP 906099 | A1 | 19990407 | <-- |
| | JP 2000504023 | T2 | 20000404 | <-- |

L31 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Preparation of heterocyclic peptide analogs as thiol-free inhibitors of farnesyl-protein transferase
 PATENT NO. KIND DATE

| | | | | |
|----|-------------|----|----------|-----|
| PI | US 5661161 | A | 19970826 | <-- |
| | WO 9610035 | A1 | 19960404 | <-- |
| | AU 9537312 | A1 | 19960419 | <-- |
| | AU 701763 | B2 | 19990204 | |
| | EP 783518 | A1 | 19970716 | <-- |
| | JP 10506900 | T2 | 19980707 | <-- |
| | ZA 9508162 | A | 19960424 | <-- |
| | US 5872135 | A | 19990216 | <-- |
| | AU 9926925 | A1 | 19990624 | <-- |

L31 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Preparation of photoreactive peptide derivatives for photoaffinity labeling of major histocompatibility complex (MHC) molecules
 PATENT NO. KIND DATE

| | | | | |
|----|------------|----|----------|-----|
| PI | WO 9702282 | A1 | 19970123 | <-- |
| | US 5827073 | A | 19981027 | |
| | CA 2225636 | AA | 19970123 | <-- |

| | | | | |
|-----|--|------|----------|-----|
| | AU 9665418 | A1 | 19970205 | <-- |
| | AU 700981 | B2 | 19990114 | |
| | EP 837876 | A1 | 19980429 | <-- |
| | JP 2000500116 | T2 | 20000111 | <-- |
| L31 | ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS | | | |
| TI | Preparation of analogs of the CAAX motif of Ras protein as inhibitors of farnesyl-protein transferase. | | | |
| | PATENT NO. | KIND | DATE | |
| | ----- | ---- | ----- | |
| PI | WO 9610035 | A1 | 19960404 | <-- |
| | US 5661161 | A | 19970826 | <-- |
| | AU 9537312 | A1 | 19960419 | <-- |
| | AU 701763 | B2 | 19990204 | |
| | EP 783518 | A1 | 19970716 | <-- |
| | JP 10506900 | T2 | 19980707 | <-- |
| | ZA 9508162 | A | 19960424 | <-- |
| L31 | ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2002 ACS | | | |
| TI | Synthetic, stabilized, three-dimension polypeptides | | | |
| | PATENT NO. | KIND | DATE | |
| | ----- | ---- | ----- | |
| PI | WO 9321206 | A1 | 19931028 | <-- |
| | AU 9339718 | A1 | 19931118 | <-- |
| | US 5807979 | A | 19980915 | <-- |
| L31 | ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2002 ACS | | | |
| TI | LHRH antagonists | | | |
| | PATENT NO. | KIND | DATE | |
| | ----- | ---- | ----- | |
| PI | WO 9213883 | A1 | 19920820 | <-- |
| | US 5171835 | A | 19921215 | <-- |
| | ZA 9200600 | A | 19921028 | <-- |
| | EP 522152 | A1 | 19930113 | <-- |
| | JP 05505630 | T2 | 19930819 | <-- |
| | HU 63635 | A2 | 19930928 | <-- |
| | NO 9304541 | A | 19940207 | <-- |
| L31 | ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2002 ACS | | | |
| TI | Preparation of LH-RH analogs as hormone-dependent neoplasm inhibitors | | | |
| | PATENT NO. | KIND | DATE | |
| | ----- | ---- | ----- | |
| PI | EP 450461 | A2 | 19911009 | <-- |
| | EP 450461 | A3 | 19920311 | |
| | EP 450461 | B1 | 19950906 | |
| | ES 2076393 | T3 | 19951101 | <-- |
| | CA 2039908 | AA | 19911007 | <-- |
| | AU 9174106 | A1 | 19911010 | <-- |
| | AU 638319 | B2 | 19930624 | |
| | HU 57235 | A2 | 19911128 | <-- |
| | JP 04224600 | A2 | 19920813 | <-- |
| | ZA 9104552 | A | 19920624 | <-- |
| | WO 9222322 | A1 | 19921223 | <-- |
| | NO 9304541 | A | 19940207 | <-- |
| L31 | ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2002 ACS | | | |
| TI | Preparation of somatostatin analogs | | | |
| | PATENT NO. | KIND | DATE | |
| | ----- | ---- | ----- | |
| PI | EP 450480 | A2 | 19911009 | <-- |

| | | | |
|-------------|----|----------|-----|
| EP 450480 | A3 | 19911218 | |
| EP 450480 | B1 | 19950621 | |
| ES 2075244 | T3 | 19951001 | <-- |
| CA 2039880 | AA | 19911007 | <-- |
| AU 9174105 | A1 | 19911010 | <-- |
| AU 638118 | B2 | 19930617 | |
| HU 59165 | A2 | 19920428 | <-- |
| JP 06041194 | A2 | 19940215 | <-- |

L31 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of aspartic acid-containing pentapeptides as antiherpes agents

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | |
|--------------|----|----------|-----|
| PI EP 411334 | A1 | 19910206 | <-- |
| EP 411334 | B1 | 19950222 | |
| CA 2019005 | AA | 19911214 | |
| IL 94980 | A1 | 19950315 | <-- |
| JP 03215497 | A2 | 19910920 | <-- |
| JP 2877909 | B2 | 19990405 | |
| AU 643636 | B2 | 19931118 | <-- |
| AU 9058775 | A1 | 19910110 | |
| US 5502036 | A | 19960326 | <-- |

L31 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of tumor necrosis factor analogs

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | |
|---------------|----|----------|-----|
| PI DE 3841755 | A1 | 19900613 | |
| WO 9006938 | A1 | 19900628 | <-- |
| EP 447431 | A1 | 19910925 | <-- |
| JP 04502307 | T2 | 19920423 | <-- |
| CA 2005056 | AA | 19900612 | <-- |

L31 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of cytotoxic LHRH analogs

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | |
|--------------|----|----------|-----|
| PI EP 364819 | A2 | 19900425 | <-- |
| EP 364819 | A3 | 19910306 | |
| JP 02157293 | A2 | 19900618 | <-- |
| US 5258492 | A | 19931102 | <-- |
| NO 9304541 | A | 19940207 | <-- |

L31 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Preparation of vasopressin fragment derivatives as nootropics for treatment of senility

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | |
|--------------|----|----------|-----|
| PI EP 227410 | A2 | 19870701 | <-- |
| EP 227410 | A3 | 19890208 | |
| US 4748154 | A | 19880531 | <-- |
| CA 1292841 | A1 | 19911203 | <-- |
| JP 62234095 | A2 | 19871014 | <-- |
| JP 08030079 | B4 | 19960327 | |

L31 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Pepstatin analogs

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

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|--------------|----|----------|-----|
| PI EP 192554 | A1 | 19860827 | <-- |
|--------------|----|----------|-----|

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|-------------|----|----------|-----|
| EP 192554 | B1 | 19920102 | |
| FR 2577225 | A1 | 19860814 | |
| FR 2577225 | B1 | 19870828 | |
| FR 2577226 | A1 | 19860814 | |
| FR 2577226 | B1 | 19900615 | |
| CA 1286846 | A1 | 19910723 | <-- |
| US 4725580 | A | 19880216 | <-- |
| US 4746648 | A | 19880524 | <-- |
| CA 1286847 | A1 | 19910723 | <-- |
| AU 8653272 | A1 | 19860814 | <-- |
| AU 606312 | B2 | 19910207 | |
| AU 8653273 | A1 | 19860821 | <-- |
| AU 606572 | B2 | 19910214 | |
| DK 8600640 | A | 19860813 | <-- |
| DK 8600641 | A | 19860813 | <-- |
| EP 193445 | A1 | 19860903 | <-- |
| EP 193445 | B1 | 19900509 | |
| ZA 8600960 | A | 19861029 | <-- |
| ZA 8600961 | A | 19861029 | <-- |
| AT 52518 | E | 19900515 | <-- |
| AT 71111 | E | 19920115 | <-- |
| ES 551820 | A1 | 19861216 | <-- |
| ES 551821 | A1 | 19870101 | <-- |
| JP 61186397 | A2 | 19860820 | <-- |
| JP 61186398 | A2 | 19860820 | <-- |

L31 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Peptides and their therapeutic use

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | | |
|----|-------------|----|----------|-----|
| PI | EP 46113 | A1 | 19820217 | <-- |
| | EP 46113 | B1 | 19841219 | |
| | FR 2488253 | A1 | 19820212 | |
| | FR 2488253 | B1 | 19840127 | |
| | US 4407794 | A | 19831004 | <-- |
| | AT 10836 | E | 19850115 | <-- |
| | CA 1292344 | A1 | 19911119 | <-- |
| | JP 57059845 | A2 | 19820410 | <-- |

L31 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI LH-RH antagonists

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | | |
|----|------------|----|----------|-----|
| PI | GB 2053229 | A | 19810204 | <-- |
| | GB 2053229 | B2 | 19830302 | |
| | US 4317815 | A | 19820302 | <-- |
| | AT 8988 | E | 19840915 | <-- |

L31 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Nouel substrates for endotoxin detection

| PATENT NO. | KIND | DATE | |
|------------|------|-------|--|
| ----- | ---- | ----- | |

| | | | | |
|----|-------------|----|----------|-----|
| PI | JP 56042597 | A2 | 19810420 | |
| | JP 63026871 | B4 | 19880531 | |
| | JP 02000192 | A2 | 19900105 | <-- |
| | JP 03011760 | B4 | 19910218 | |

L31 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 TI Blocking allergic responses

| PATENT NO. | KIND | DATE | |
|------------|------|------|--|
|------------|------|------|--|

| | | | | |
|----|------------|----|----------|-----|
| PI | US 4161522 | A | 19790717 | <-- |
| | US 4171299 | A | 19791016 | <-- |
| | AU 8065181 | A1 | 19810416 | <-- |
| | AU 531075 | B2 | 19830811 | |

L31 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Tetrapeptides and their preparation and use in determining serine proteases

| | PATENT NO. | KIND | DATE | |
|----|-------------|------|----------|-----|
| PI | DE 2753653 | A1 | 19780608 | <-- |
| | DE 2753653 | C2 | 19830721 | |
| | SE 7613463 | A | 19780602 | |
| | SE 437153 | B | 19850211 | |
| | SE 437153 | C | 19850530 | |
| | IL 53187 | A1 | 19810227 | <-- |
| | NL 7711791 | A | 19780605 | <-- |
| | NL 178600 | B | 19851118 | |
| | NL 178600 | C | 19860416 | |
| | FI 7703242 | A | 19780602 | <-- |
| | ZA 7706460 | A | 19780830 | <-- |
| | ES 464117 | A1 | 19780901 | <-- |
| | US 4207232 | A | 19800610 | <-- |
| | AU 7730771 | A1 | 19790524 | <-- |
| | AU 514768 | B2 | 19810226 | |
| | GB 1565154 | A | 19800416 | <-- |
| | BE 861295 | A1 | 19780316 | <-- |
| | FR 2372798 | A1 | 19780630 | <-- |
| | FR 2372798 | B1 | 19831110 | |
| | DD 136896 | C | 19790801 | <-- |
| | PL 109588 | B1 | 19800630 | <-- |
| | CH 637627 | A | 19830815 | <-- |
| | NO 7704092 | A | 19780602 | <-- |
| | SU 736889 | D | 19800525 | <-- |
| | CA 1098428 | A1 | 19810331 | <-- |
| | DK 7705353 | A | 19780602 | <-- |
| | DK 155333 | B | 19890328 | |
| | DK 155333 | C | 19890904 | |
| | JP 53069693 | A2 | 19780621 | <-- |
| | JP 57008720 | B4 | 19820217 | |
| | AT 7708596 | A | 19800115 | <-- |
| | AT 358203 | B | 19800825 | |
| | HU 19255 | O | 19801227 | <-- |
| | HU 176983 | P | 19810628 | |
| | DE 2760116 | C2 | 19850912 | <-- |
| | US 4276375 | A | 19810630 | <-- |

L31 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2002 ACS

TI Biologically active polypeptides

| | PATENT NO. | KIND | DATE | |
|----|-------------|------|----------|-----|
| PI | DE 2602443 | A1 | 19761021 | <-- |
| | JP 51118702 | A2 | 19761018 | <-- |
| | JP 60002318 | B4 | 19850121 | |
| | AU 7612303 | A1 | 19770929 | <-- |
| | AU 514308 | B2 | 19810205 | |
| | GB 1539102 | A | 19790124 | <-- |
| | BE 840193 | A1 | 19760930 | <-- |
| | FR 2305989 | A1 | 19761029 | <-- |

CANELLA 09/544,644

| | | | |
|------------|----|----------|-----|
| FR 2305989 | B1 | 19791005 | |
| CA 1087171 | A1 | 19801007 | <-- |
| SE 7603897 | A | 19761005 | <-- |
| SE 430058 | B | 19831017 | |
| SE 430058 | C | 19840126 | |
| NL 7603384 | A | 19761006 | <-- |
| CH 624093 | A | 19810715 | <-- |
| CA 1079721 | A2 | 19800617 | <-- |
| AU 8065181 | A1 | 19810416 | <-- |
| AU 531075 | B2 | 19830811 | |

=> d ibib abs hitstr 5,7,9-14,17-28

L31 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:84834 HCAPLUS

DOCUMENT NUMBER: 132:137733

TITLE: Preparation of new antifungal agents, cyclic
aerothricin analogs, for treatment of infectious
diseases caused by pathogenic microorganisms

INVENTOR(S): Aoki, Masahiro; Kohchi, Masami; Masubuchi, Kazunao;
Mizuguchi, Eisaku; Murata, Takeshi; Ohkuma, Hiroaki;
Okada, Takehiro; Sakaitani, Masahiro; Shimma, Nobuo;
Watanabe, Takahide; Yanagisawa, Mieko; Yasuda, Yuri

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

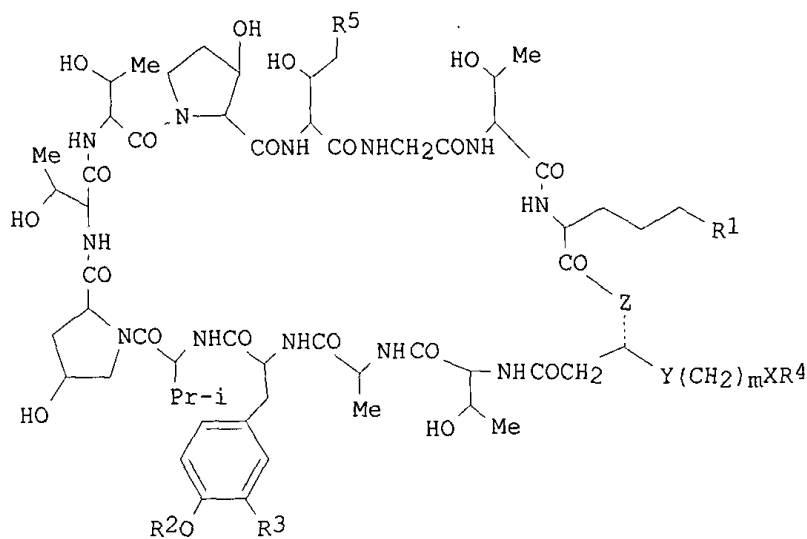
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2000005251 | A1 | 20000203 | WO 1999-EP5235 | 19990722 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9951630 | A1 | 20000214 | AU 1999-51630 | 19990722 <-- |
| BR 9912367 | A | 20010502 | BR 1999-12367 | 19990722 <-- |
| EP 1100816 | A1 | 20010523 | EP 1999-936588 | 19990722 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | EP 1998-113744 | A 19980723 <-- |
| | | | EP 1999-107637 | A 19990416 <-- |
| | | | WO 1999-EP5235 | W 19990722 |

OTHER SOURCE(S): MARPAT 132:137733

GI



I

AB Novel antifungal aerothricins I [R1 = guanidino, trialkylammonio, NR10R11, NR15COR14, NR15COCH(NR10R11)R13 (Q), NHCOCHR13NHCOCH(NH2)R13, N[(CH2)nQ]2, N[(CH2)nQ][COCH(NR10R11)R13], or NR15COR12, where n = 2-5, R10, R11 = H, heteroaryl or mono- or diaminoheteroaryl, alkyl optionally substituted with one or more amino groups, aminoalkyl, cyano, guanidino, nitrogen-contg. heterocycle(s) or Ph group(s) contg. an amino, amidino or guanidino group, R12 is tetrahydro-2-pyrrolyl optionally substituted at N by R10 and by an amino group, R13 is a residue from natural or unnatural amino acids, R14 is alkyl substituted with one or more amino, guanidino, nitrogen contg. heterocycle or Ph group contg. an amino, amidino, or guanidino group, and R15 = H or R14-like group; R2 = H, HOSO2, alkyl or alkenyl optionally substituted with acyl, carbamoyl, amino, mono- or dialkylamino; R3 = H, OH, NO2, NH2, acylamino, (alkylcarbamoyl)amino, carboxyl, alkoxy, alkoxy-carbonyl, (un)substituted alkyl, alkenyl, or alkynyl; R4 = alkyl, alkenyl, alkoxy or alkenyloxy optionally substituted with alkyl, aryl, cycloalkyl or F; R5 = CONH2, CN, CH2NH2; X is a single bond, aryl, biphenyl, terphenyl optionally contg. one or more heteroatom(s) and/or substituted with halo or alkyl; Y is a single bond, CH2, CH(alkyl), CONH, CON(alkyl); Z = O, NH, alkylamino; m = 0-4 (with provisos)] and pharmaceutically acceptable salts were prepd. Numerous processes for the prepn. of aerothricins of formula I are described. Thus, aerothricin 3 [I; R1 = NH2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me] (WF11243), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions in aq. medium, was treated with (2-oxoethyl)carbamic acid tert-Bu ester in MeOH in the presence of sodium cyanoborohydride and acetic acid to afford aerothricin 111 [I; R1 = N(CH2CH2NH2)2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me]. The aerothricins of formula I as well as pharmaceutically acceptable salts exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized aerothricins are less cytotoxic to hepatocytes than the known cyclic peptide derivs., e.g., WF11243.

IT 256947-24-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of)

RN 256947-24-7 HCAPLUS
 CN Cyclo[alanyltyrosylvalyl-4-hydroxyprolylthreonylthreonyl-3-hydroxyprolyl-3-hydroxyglutaminyglycylthreonyl-N5-[3-[[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanyl]ornithyl-(3R)-3-hydroxyhexadecanoylthreonyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:161129 HCAPLUS

DOCUMENT NUMBER: 128:230693

TITLE: Preparation of novel cryptophycin pharmaceuticals

INVENTOR(S): Al-Awar, Rima S.; Ehlhardt, William J.; Gottumukkala, Subbaraju V.; Martinelli, Michael J.; Moher, Eric D.; Moore, Richard E.; Munroe, John E.; Norman, Bryan H.; et al.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; University of Hawaii; Wayne State University; Al-Awar, Rima S.; Ehlhardt, William J.; Gottumukkala, Subbaraju V.; Martinelli, Michael J.; Moher, Eric D.

SOURCE: PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

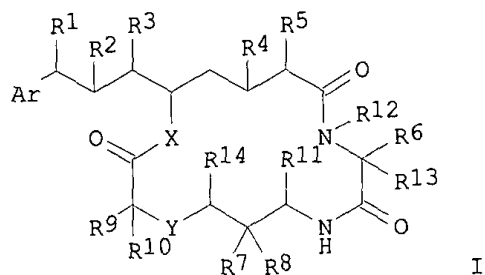
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| WO 9808505 | A1 | 19980305 | WO 1997-US15240 | 19970829 <-- |
| W: | | | | |
| AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: | | | | |
| GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9741701 | A1 | 19980319 | AU 1997-41701 | 19970829 <-- |
| AU 722492 | B2 | 20000803 | | |
| EP 934065 | A1 | 19990811 | EP 1997-939667 | 19970829 <-- |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9711986 | A | 19990824 | BR 1997-11986 | 19970829 <-- |
| CN 1233957 | A | 19991103 | CN 1997-199082 | 19970829 <-- |
| NO 9900833 | A | 19990426 | NO 1999-833 | 19990222 <-- |
| PRIORITY APPLN. INFO.: | | | US 1996-25816P | P 19960830 <-- |
| | | | US 1997-39113P | P 19970226 <-- |
| | | | US 1997-39530P | P 19970303 <-- |
| | | | US 1997-40029P | P 19970304 <-- |
| | | | WO 1997-US15240 | W 19970829 <-- |

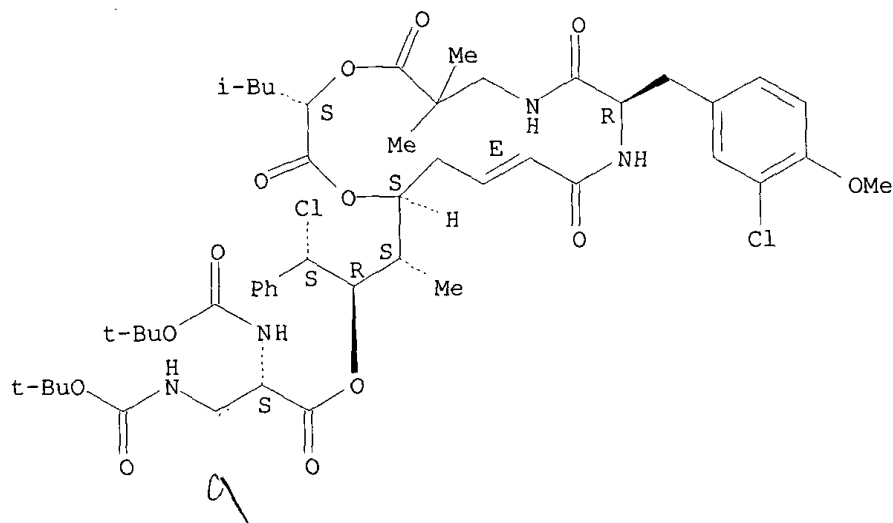
OTHER SOURCE(S): MARPAT 128:230693

GI



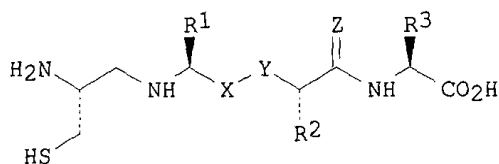
- AB Cryptophycin compds. I [Ar = Ph, (un)substituted aryl or heteroaryl, heterocyclyl, etc.; R1 and R1 may form a ring or a bond; R3 = alkyl; R4, R5 = H, OH or together may form a second bond; R6 = (un)substituted benzyl, heteroaryl, cycloalkyl, etc.; R7 = alkylamino, alkoxy, H, alkyl; R8 = H, alkyl; R7 and R8 can form a cyclopropyl group; R9 = H, alkyl, alkenyl, alkylcycloalkyl, benzyl; R10 = H, alkyl; R11 = H, OH, alkyl, (un)substituted benzyl or phenyl; R12 = H, alkyl; R13 = may form a ring with the adjacent nitrogen atom; R14 = H, CO; X = O, C, S, NH, alkylamino; Y = C, O, NH, S, SO₂, alkylamino] were prepd. as antineoplastic agents. Thus, cryptophycin 55 acetate (LSN 362376) was prepd. and assayed for in vivo toxicity in the Gc3 tumor cell model (IC₅₀ = 83 nM).
- IT **204446-46-8P**, LSN 382765
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of novel cryptophycin pharmaceuticals)
- RN 204446-46-8 HCAPLUS
- CN Pentanoic acid, 3-chloro-N-[(2E,5S,6S,7R,8S)-8-chloro-5,7-dihydroxy-6-methyl-1-oxo-8-phenyl-2-octenyl]-O-methyl-D-tyrosyl-2,2-dimethyl-.beta.-alanyl-2-hydroxy-4-methyl-, (3.fwdarw.15)-lactone, 17-ester with N-[(1,1-dimethylethoxy)carbonyl]-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanine, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



ACCESSION NUMBER: 1997:696611 HCAPLUS
 DOCUMENT NUMBER: 127:359110
 TITLE: Preparation of transferase inhibitors for treating cancer
 INVENTOR(S): Gibbs, Jackson B.; Kohl, Nancy E.; Oliff, Allen I.
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Gibbs, Jackson B.; Kohl, Nancy E.; Oliff, Allen I.
 SOURCE: PCT Int. Appl., 301 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 9738664 | A2 | 19971023 | WO 1997-US6248 | 19970415 <-- |
| WO 9738664 | A3 | 19971120 | | |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2251955 | AA | 19971023 | CA 1997-2251955 | 19970415 <-- |
| AU 9728022 | A1 | 19971107 | AU 1997-28022 | 19970415 <-- |
| EP 952842 | A2 | 19991103 | EP 1997-922313 | 19970415 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2000513711 | T2 | 20001017 | JP 1997-537313 | 19970415 <-- |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1996-15589P | P 19960418 <-- |
| | | | GB 1996-11982 | A 19960607 <-- |
| | | | WO 1997-US6248 | W 19970415 <-- |
| OTHER SOURCE(S): MARPAT 127:359110 | | | | |
| GI | | | | |



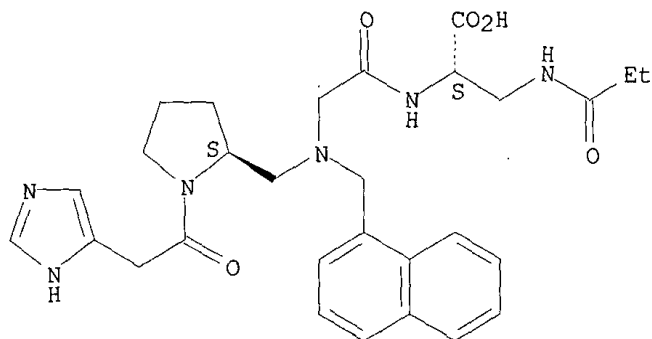
I

- AB Geranylgeranyl-protein transferase-type I (GGPTase-I) and farnesyl protein transferase (FTase) inhibitors I [R1, R2 = (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, or side chain of a naturally occurring amino acid; R3 = alkyl, alkenyl, or alkynyl which are optionally substituted by a Ph group; X-Y = CONH, CH2O, or CH:CH; Z = H2, O] were prep'd. for treating cancer. Thus, N-[N-[N-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]pyrrolidin-2(S)-ylmethyl]-3(S)-ethylprolyl]methionine iso-Pr ester was prep'd. and assayed for transferase inhibitory activity [IC50 = 1.8 nM (FPTase) and 3000 nM (GGPTase-I)].
- IT 179014-32-5P 179014-33-6P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of transferase inhibitors for treating cancer)

RN 179014-32-5 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

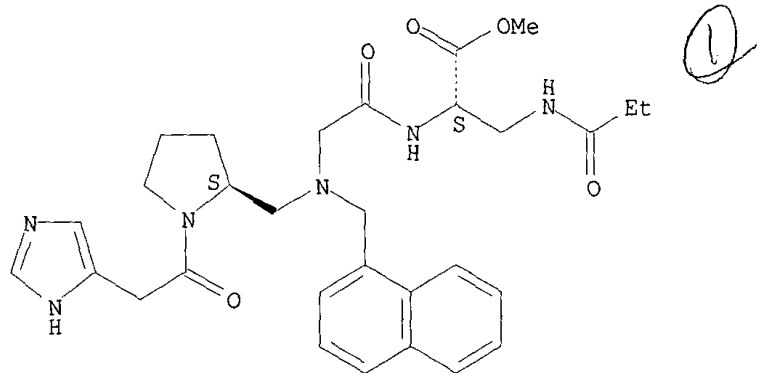
Absolute stereochemistry.



RN 179014-33-6 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:672274 HCAPLUS

DOCUMENT NUMBER: 127:331747

TITLE: Preparation of imidazole derivatives and imidazole-contg. peptide analogs and a method of treating cancer

INVENTOR(S): Heimbrook, David C.; Oliff, Allen I.; Stirdivant, Steven M.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Heimbrook, David C.; Oliff, Allen I.; Stirdivant, Steven M.

SOURCE: PCT Int. Appl., 313 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|----------------|
| WO 9736587 | A1 | 19971009 | WO 1997-US5328 | 19970331 <-- |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2250232 | AA | 19971009 | CA 1997-2250232 | 19970331 <-- |
| AU 9727221 | A1 | 19971022 | AU 1997-27221 | 19970331 <-- |
| AU 727939 | B2 | 20010104 | | |
| EP 906099 | A1 | 19990407 | EP 1997-921085 | 19970331 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2000504023 | T2 | 20000404 | JP 1997-535542 | 19970331 <-- |
| PRIORITY APPLN. INFO.: | | | US 1996-14773P | P 19960403 <-- |
| | | | GB 1996-13599 | A 19960628 <-- |
| | | | WO 1997-US5328 | W 19970331 <-- |
| OTHER SOURCE(S): | | | MARPAT 127:331747 | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to a method of treating cancer which comprises administering to a mammalian patient a compd. which inhibits Raf (a Raf antagonist) and a compd. which inhibits farnesyl protein transferase. The cancer to be treated is selected from the brain, genitourinary tract, lymphatic system, stomach, larynx, and lung. The Raf antagonists are represented by formula [e.g. I; AR = arom. group contg. 6-10 atoms; X, X1 = (CH₂)_m-Y-(CH₂)_n; wherein m, n = 0-4 and m+n = 0-6; Y = a direct bond, O, S, SO, SO₂, (un)substituted NH, SONH, SO₂NH, NHSO, NHSO₂, CONH, or NHCO, CO, CO₂, O₂C; "HET" ring = 4- to 10-membered non-arom. heterocyclic ring contg. at least 1 N and optionally contg. 1-2 addnl. N atoms and 0-1 O or S atom; Rx = H, C1-6 alkyl(Rq)3, O-C1-6 alkyl(Rq)3, CO-C1-6 alkyl(Rq)3; R, R' = halo, OH, C1-6 alkyl(Rq)3, O-C1-6 alkyl(Rq)3, C3-8 cycloalkyl(Rq)3, cyano, (un)substituted CONH₂ or NH₂, CO₂H or its alkyl ester, CF₃, SH, NO₂, (un)substituted SO₂NH₂, etc.; R' = (un)substituted CONH₂, CO₂H or its (cyclo)alkyl ester, CO C3-8 cycloalkyl(Rq)3, CO-C3-8 cycloalkyl(Rq)3, CO-heterocyclyl(Rq)3, CO-(hetero)aryl(Rq)3, etc.; wherein Rq = H, OH, C1-4 alkoxy, aryl, C1-4 alkyl-carbonyl, cyano, CO₂H, C1-4 alkoxycarbonyl, C1-4 alkylcarbonyl, (un)substituted NH₂, etc.]. The farnesyl protein transferase inhibitors are represented by formula [e.g. II; R = (R₈)r-V-Al[C(R1a)₂]nA₂[C(R1a)₂]n-(WR₉)t-[C(R1b)]p; R1a, R1b = H, aryl, heterocyclyl, C3-10 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, (un)substituted OH, cyano, NO₂, (un)substituted C1-6 alkyl, etc.; R₂, R₃ = H, (un)substituted C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, aryl, heterocyclyl, CONH₂, CO₂H, NH₂, NHCONH₂, or O₂CNH₂, etc.; R₄, R₅ = H, Me; R₈ = H, aryl, heterocyclyl, C3-10 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, perfluoroalkyl, F, Cl, Br, (un)substituted OH, acylamino, cyano, NO₂, (un)substituted C(:NH)NH₂, acyl, (un)substituted CO₂H, N₃, (un)substituted NH₂, etc.; R₉ = H, C2-6 alkenyl, C2-6 alkynyl, perfluoroalkyl, F, Cl, Br, (un)substituted OH, acylamino, cyano, NH₂, (un)substituted C(:NH)NH₂,

acyl, (un)substituted CO₂H, N₃, (un)substituted NH₂, (un)substituted C1-6 alkyl, etc.; A1, A2 = a bond, CH:CH, C.tplbond.C, CO, (un)substituted CONH, NHCO, NH, SO₂NH, NHSO₂, S, SO, SO₂; V = H, heterocyclyl, aryl, C1-20 alkyl (wherein 0-4 c atoms are replaced with a heteroatom selected from O, S, and N), C2-20 alkyl; W = heterocycle; X = CH₂, CO, S, SO, SO₂; Y = (un)substituted aryl or heterocyclyl; n, p = 0, 1-4; r = 0-5; m, t = 0, 1]. They are also represented by peptide analog of formula [e.g. III; R = (R₈)r-V-A1[C(R1a)2]nA2[C(R1a)2]n-(WR₉)u-[C(R1b)]p; R1a, R1b, V, W, n, p, r = same as above; R2a, R2b = H, (un)substituted C1-6 alkyl, aryl, heterocyclyl, C3-10 cycloalkyl, C2-6 alkenyl, (un)substituted OH, acylamino, cyano, NO₂, H₂NC(:NH), acyl, (un)substituted CO₂H, N₃, (un)substituted NH₂, etc.; R₃, R₄, R_{5a}, R_{5b} = a side chain of a naturally occurring amino acid, methionine sulfoxide, or methionine sulfone, (un)substituted C1-20 alkyl, C2-20 alkenyl, C3-10 cycloalkyl, aryl, or heterocyclyl, etc.; or R₃R₄ = (CH₂)₄ or 5; or R_{5a}R_{5b} = (CH₂)₄ or 5 wherein one of the C atoms is optionally replaced by O, S, SO, SO₂, N-CO, and N-acyl-NH; X-Y = N-(un)substituted CONH or CH₂NH, CH₂O, CH₂S, CH₂SO, CH₂SO₂, trans-CH:CH, CH₂CH₂; R₈ = H, aryl, heterocyclyl, C3-10 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, perfluoroalkyl F, Cl, Br, (un)substituted OH, acylamino, cyano, NO₂, (un)substituted H₂NC(:NH), acyl, (un)substituted CO₂H, N₃, (un)substituted NH₂, (un)substituted C1-6 alkyl, etc.; R₉ = H, C2-6 alkenyl, C2-6 alkynyl, perfluoroalkyl, F, Cl, Br, (un)substituted OH, acylamino, cyano, NO₂, H₂NC(:NH), acyl, (un)substituted CO₂H, N₃, (un)substituted NH₂, (un)substituted C1-6 alkyl etc.; Z = H₂, O; u = 0,1; m = 3,4,5]. Thus, 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride was condensed with N-[2(S)-amino-3(S)-methylphenyl]-N-(naphthylmethyl)glycyl-L-methionine Me ester dihydrochloride using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 3-hydroxy-1,2,3-benzotriazin-4(3H)-one in CH₂Cl₂ at room temp. overnight to give a peptide deriv. (III; R = NO₂), which was converted into the 4-cyano deriv. III (R = cyano).

IT 179014-32-5P 179014-33-6P

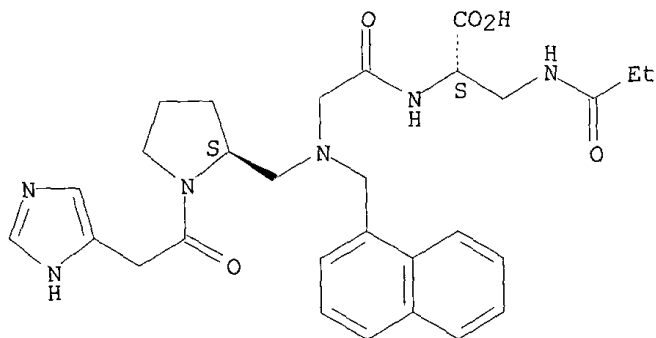
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of imidazole derivs. as Raf protein antagonists and imidazole-contg. peptide analogs as farnesyl protein transferase inhibitors for treating cancer)

RN 179014-32-5 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

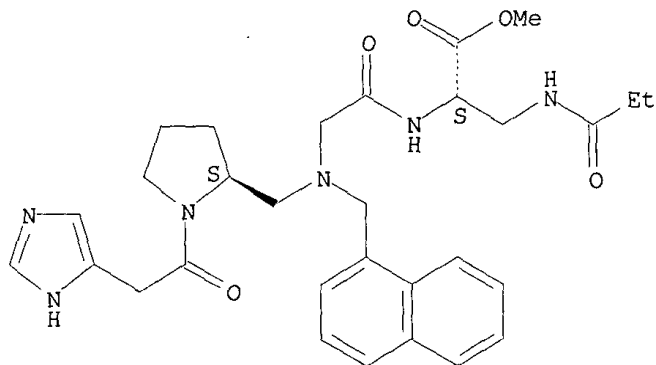
Absolute stereochemistry.



RN 179014-33-6 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

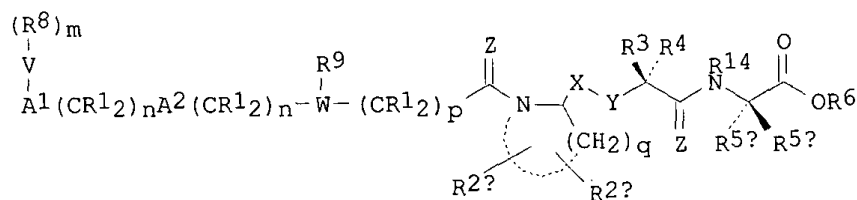


L31 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:576604 HCAPLUS
 DOCUMENT NUMBER: 127:248418
 TITLE: Preparation of heterocyclic peptide analogs as thiol-free inhibitors of farnesyl-protein transferase
 INVENTOR(S): Anthony, Neville J.; Ciccione, Terrence M.; Desolms, S. Jane; Graham, Samuel L.; Stokker, Gerald E.; Wiscount, Catherine M.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: U.S., 73 pp. Cont.-in-part of U.S. Ser. No. 472,077, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

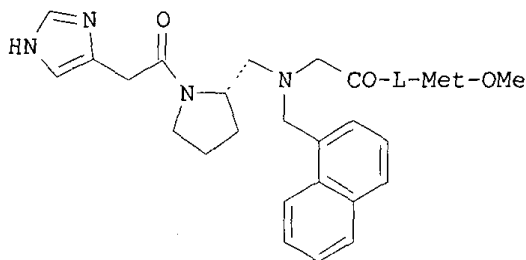
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| US 5661161 | A | 19970826 | US 1995-527972 | 19950914 <-- |
| WO 9610035 | A1 | 19960404 | WO 1995-US12474 | 19950927 <-- |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, US, US, US, UZ | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9537312 | A1 | 19960419 | AU 1995-37312 | 19950927 <-- |
| AU 701763 | B2 | 19990204 | | |
| EP 783518 | A1 | 19970716 | EP 1995-935199 | 19950927 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 10506900 | T2 | 19980707 | JP 1995-512037 | 19950927 <-- |
| ZA 9508162 | A | 19960424 | ZA 1995-8162 | 19950928 <-- |
| US 5872135 | A | 19990216 | US 1997-824936 | 19970326 <-- |
| AU 9926925 | A1 | 19990624 | AU 1999-26925 | 19990504 <-- |
| PRIORITY APPLN. INFO.: | | | US 1994-315161 | 19940929 <-- |
| | | | US 1995-399282 | 19950306 <-- |

| | |
|-----------------|--------------|
| US 1995-472077 | 19950606 <-- |
| US 1995-527972 | 19950914 <-- |
| AU 1995-37312 | 19950927 <-- |
| WO 1995-US12474 | 19950927 <-- |

OTHER SOURCE(S): MARPAT 127:248418
GI



I



II

AB Peptide analogs I [R1 = H, aryl, heterocyclyl, cycloalkyl, alkenyl, alkynyl, (un)substituted C1-6 alkyl, etc.; R2a, R2b, R3, R4, R5a, R5b = amino acid side chain, CH₂CH₂S(O)Me, CH₂CH₂SO₂Me, (un)substituted C1-20 alkyl, C2-20 alkenyl, C3-10 cycloalkyl, aryl, heterocyclyl, etc.; or R2aR2b or R3R4 form -(CH₂)_s-; or R5aR5b form -(CH₂)_s- wherein one of the C atoms is replaced by O, S(O)t, NC(O), N-acylamino, wherein s = 4 or 5, t = 0-2; or R5aR5b form a ring with R14; X-Y = N-(un)substituted CONH, CH₂NH, CH₂O, CH₂S(O)t, trans-CH:CH; R6 = H, C1-6 alkyl, C1-8 alkyl substituted with aryl, heterocyclyl, N(R11)₂, OR10, etc.; R5aR6 form 5-7 membered lactone ring; R8 = H, aryl, heterocyclyl, alkenyl, perfluoroalkyl, F, CN, NO₂, (un)substituted C1-6 alkyl, etc.; R9 = H, alkenyl, perfluoroalkyl, Cl, Br, N3, CN, (un)substituted C1-6 alkyl, etc.; R10 = H, C1-6 alkyl, aryl; R11 = C1-6 alkyl, aryl; R14 = H, C1-6 alkyl, benzyl; A1, A2 = bond, CH:CH, C.tplbond.C, O, CO, N-(un)substituted NH, CONH, S(O)2NH, S(O)t, etc., V = H, aryl, heterocyclyl, C1-20 alkyl with 0-4 non-terminal atoms replaced with O, S, N; C2-20 alkenyl; W = heterocyclyl or W-R9 = absent; Z = H2, O; n, p = 0-4; m = 0-5; q = 3-5] of the CAAX motif of the protein RAS that is modified by farnesylation in vivo are prep'd. These CAAX analogs inhibit farnesyl-protein transferase. Furthermore, these CAAX analogs differ from those previously described as inhibitors of farnesyl-protein transferase in that they do not have a thiol moiety. The lack of the thiol offers unique advantages in terms of improved pharmacokinetic behavior in animals, prevention of thiol-dependent chem. reactions, such as rapid autoxidn. and disulfide formation with endogenous thiols, and reduced systemic toxicity. Further contained in this invention are chemotherapeutic compns. contg. these farnesyl transferase inhibitors and methods for their prodn. Thus, sequential reductive alkylations of H-Gly-OMe.HCl with N-tert-butoxycarbonyl-L-prolinal and 1-naphthaldehyde, followed by sapon., peptide coupling with H-Met-OMe.HCl,

deprotection, and amidation with 4-imidazoleacetic acid hydrochloride, gave reduced bond peptidomimetic II. II and related compds. showed in vitro inhibition of human farnesyltransferase with IC₅₀ <10 .mu.M.

IT 179014-32-5 179014-33-6

RL: BAC (Biological activity or effector, except adverse); THU .

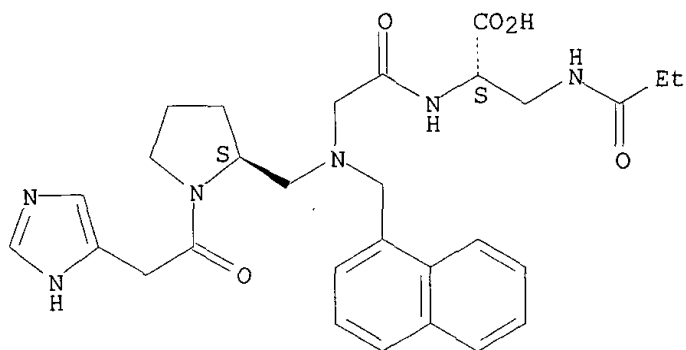
(Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of heterocyclic peptide analogs as thiol-free inhibitors of farnesyl-protein transferase)

RN 179014-32-5 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

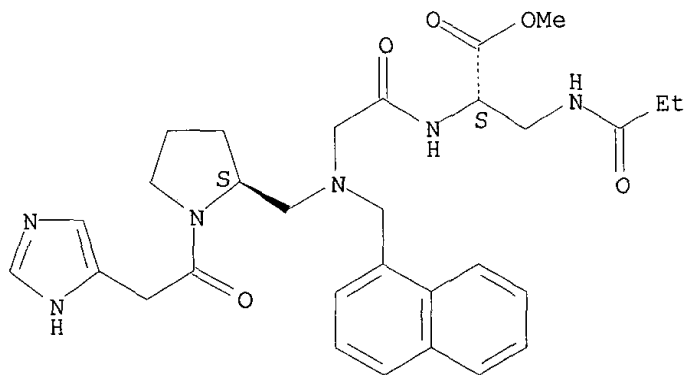
Absolute stereochemistry.



RN 179014-33-6 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:195727 HCAPLUS

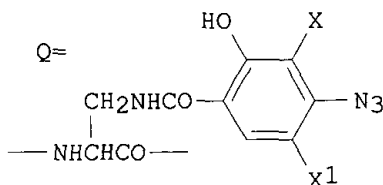
DOCUMENT NUMBER: 126:199837

TITLE: Preparation of photoreactive peptide derivatives for photoaffinity labeling of major histocompatibility complex (MHC) molecules

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 PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 9702282 | A1 | 19970123 | WO 1996-US10869 | 19960625 <-- |
| W: AU, CA, CN, FI, JP, NO, NZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5827073 | A | 19981027 | US 1995-498461 | 19950705 |
| CA 2225636 | AA | 19970123 | CA 1996-2225636 | 19960625 <-- |
| AU 9665418 | A1 | 19970205 | AU 1996-65418 | 19960625 <-- |
| AU 700981 | B2 | 19990114 | | |
| EP 837876 | A1 | 19980429 | EP 1996-925264 | 19960625 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000500116 | T2 | 20000111 | JP 1997-505187 | 19960625 <-- |
| PRIORITY APPLN. INFO.: | | | US 1995-498461 | 19950705 <-- |
| | | | WO 1996-US10869 | 19960625 <-- |

GI



AB This invention relates to a method of producing synthetic photoreactive peptide derivs., which involves (a) producing a synthetic peptide using linear synthesis, (b) substituting an amino acid of said peptide with a photoreactive amino acid at a position such that said photoreactive amino acid does not change the binding abilities of said peptide, and (c) specifically radioiodinating said photoreactive amino acid. These photoreactive peptide derivs. can be used to det. whether specific peptides are able to bind to specific MHC mols. Thus, a photoreactive deriv. of the melanoma derived MAGE-1 peptide 161-169 (EADPTGHSY), i.e. H-EADPTGDap(ASA)SY(PO3H2)-OH [I; Dap(ASA)= N.beta.-(4-azidosalicyloyl)-2,3-diaminopropionic acid residue (Q), wherein X = X1 = H], was synthesized by conventional solid phase peptide synthesis based on the Fmoc strategy using Fmoc-Dap(ASA)-OH (wherein X = X1 = H prepn. given) and Fmoc-Tyr(PO3H2)-OH and was next subjected to iodination with NaI and chloramine T and then dephosphorylated with alk. phosphatase to give a mixt. of 3-iodinated H-EADPTGDap(ASA)SY-OH (II; X = iodo, X1 = H), 5-iodinated II (X = H, X1 = iodo), and 3,5-diiodinated II (X = X1 = iodo). 125I-radiolabeled II was similarly prepd. by iodination of I (X = X1 = H) with Na125I and chloramine T followed by dephosphorylation and was incubated with HLA-A1 transfected CIR cells in the presence of .beta.2-microglobulin and irradiated with UV using a 15 W mercury fluorescence lamp to show remarkable specificity for photoaffinity

labeling of mols. HLA-A1 and lack of significant labeling of other cellular components.

IT 167695-13-8P 187603-67-4P 187603-68-5P
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RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

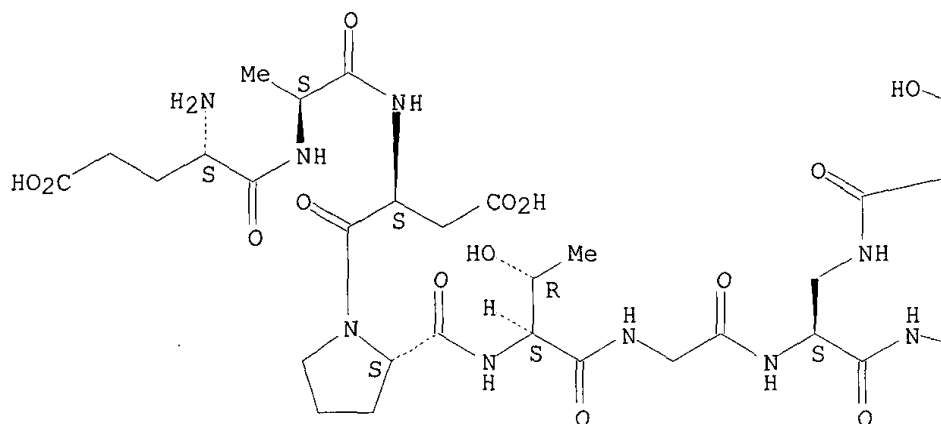
(prepn. of photoreactive peptide derivs. for photoaffinity labeling of major histocompatibility complex (MHC) mols.)

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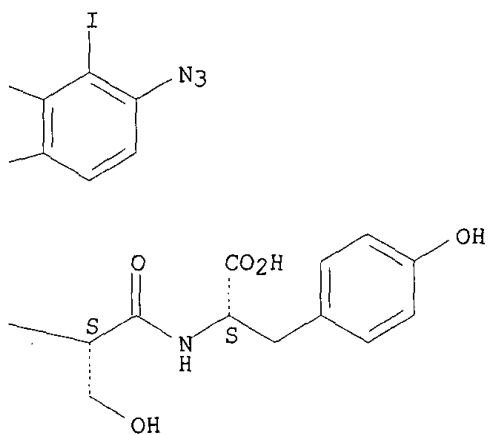
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Absolute stereochemistry.

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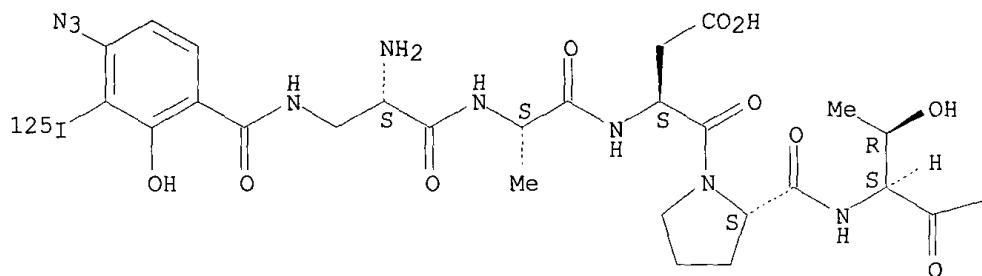


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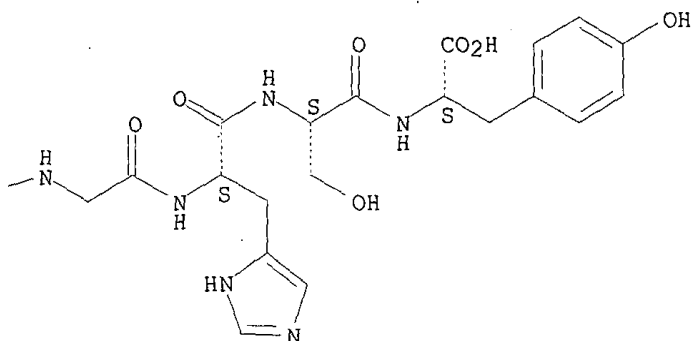
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Absolute stereochemistry.

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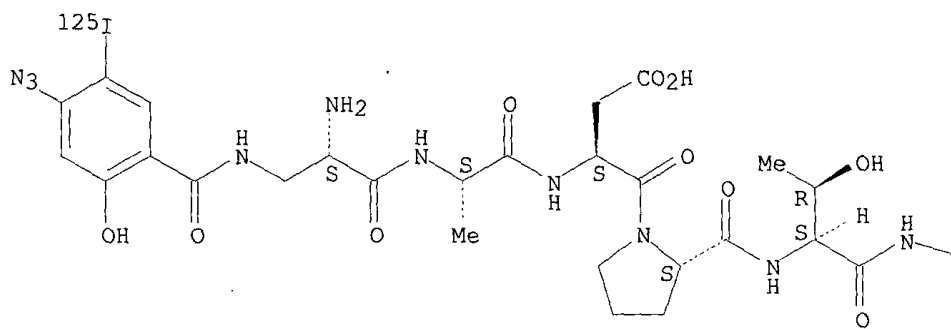


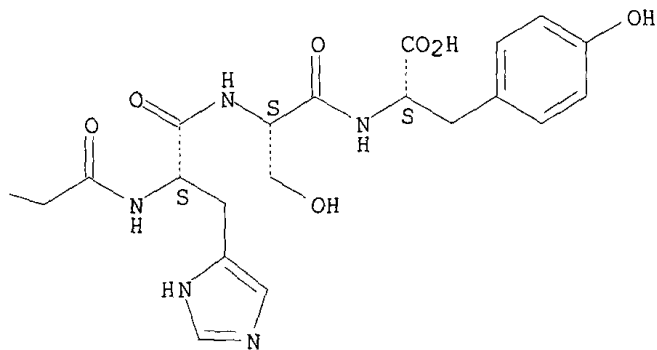
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Absolute stereochemistry.

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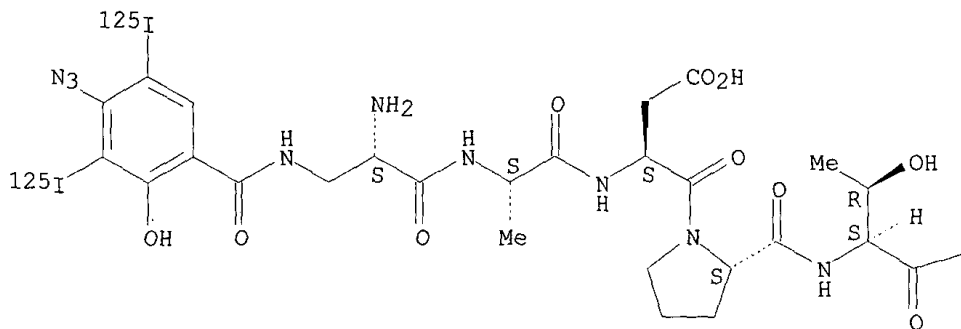


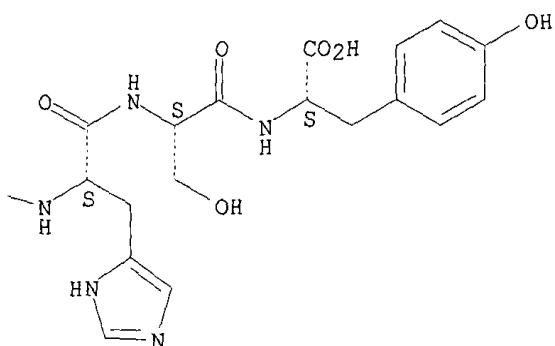


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Absolute stereochemistry.

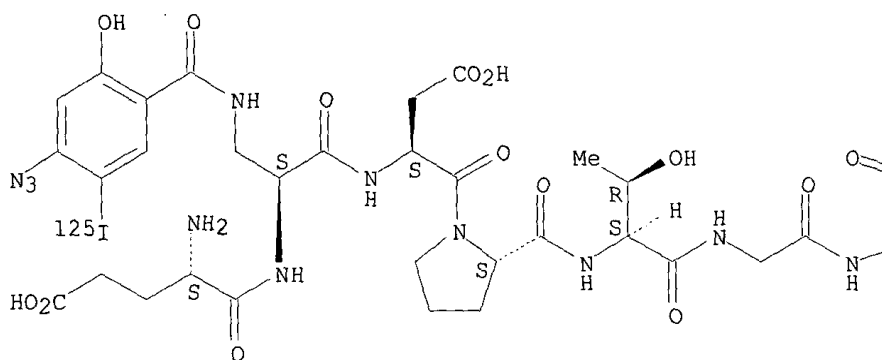


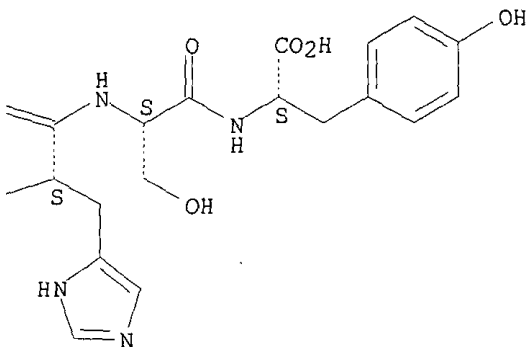


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Absolute stereochemistry.

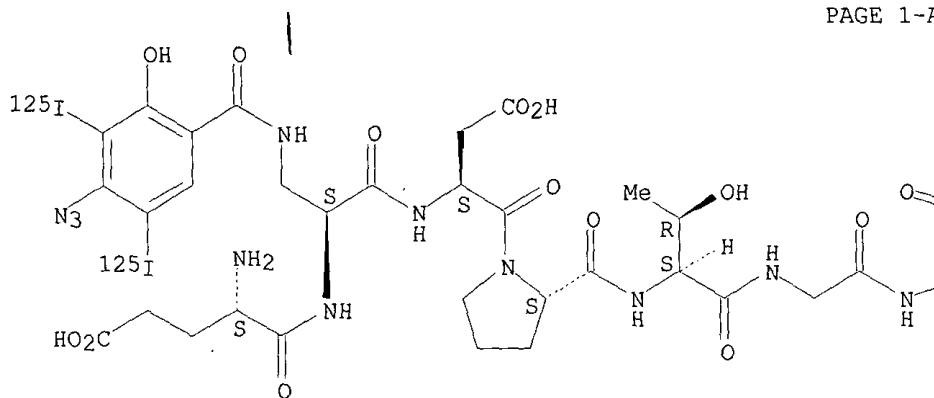


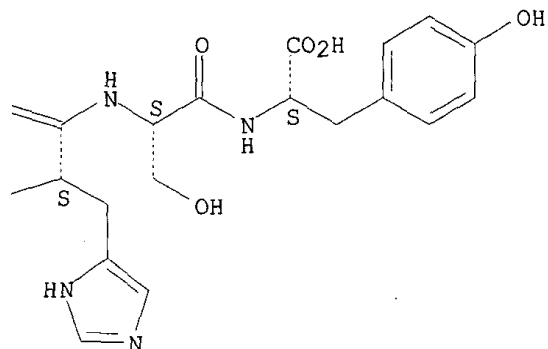


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Absolute stereochemistry.

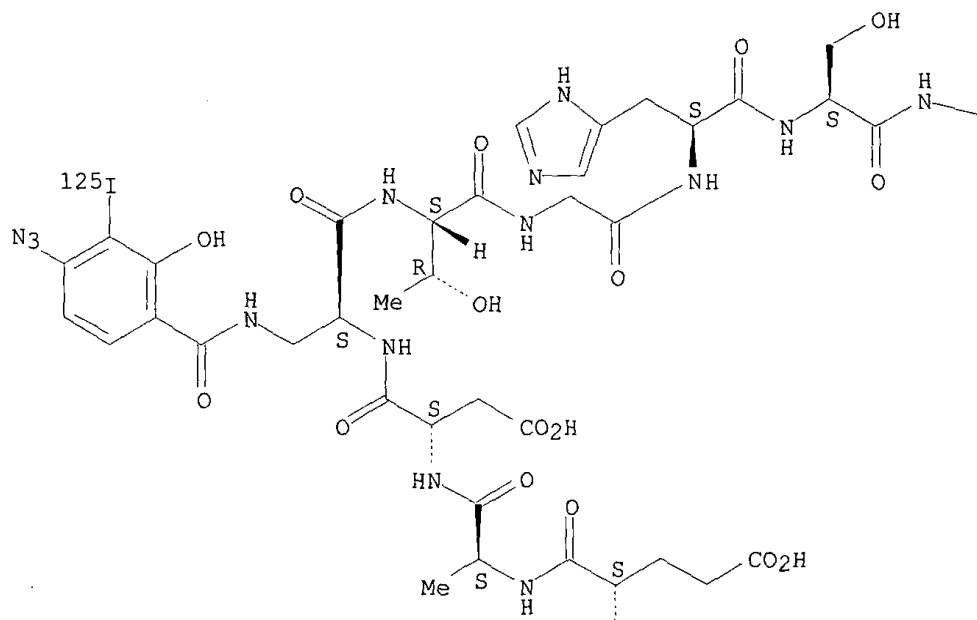




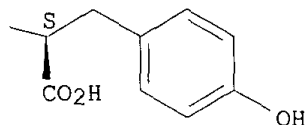
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Absolute stereochemistry.



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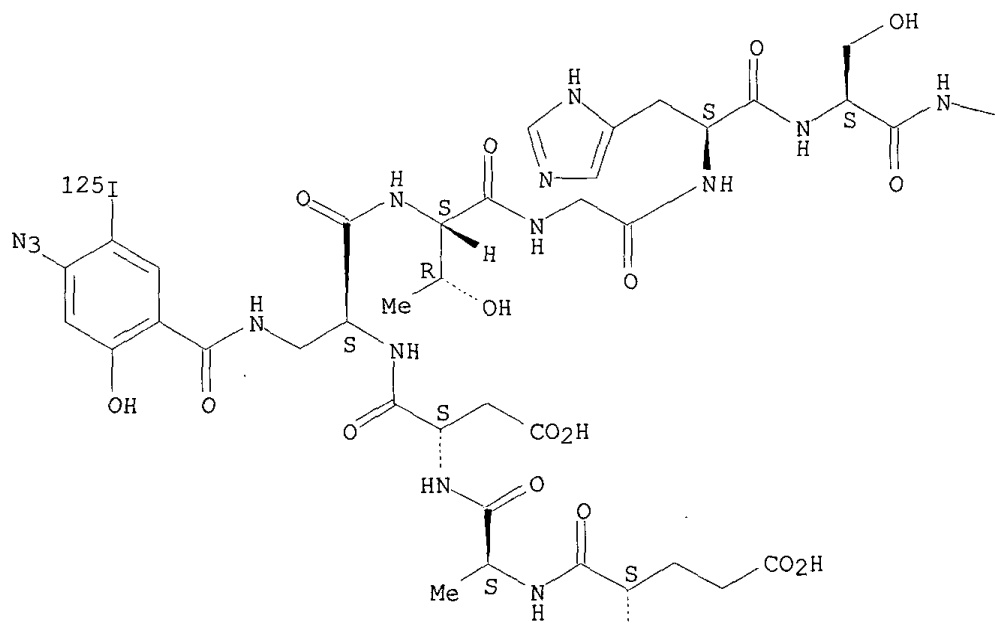


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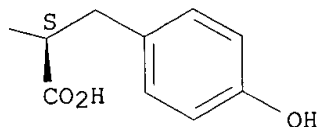
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Absolute stereochemistry.

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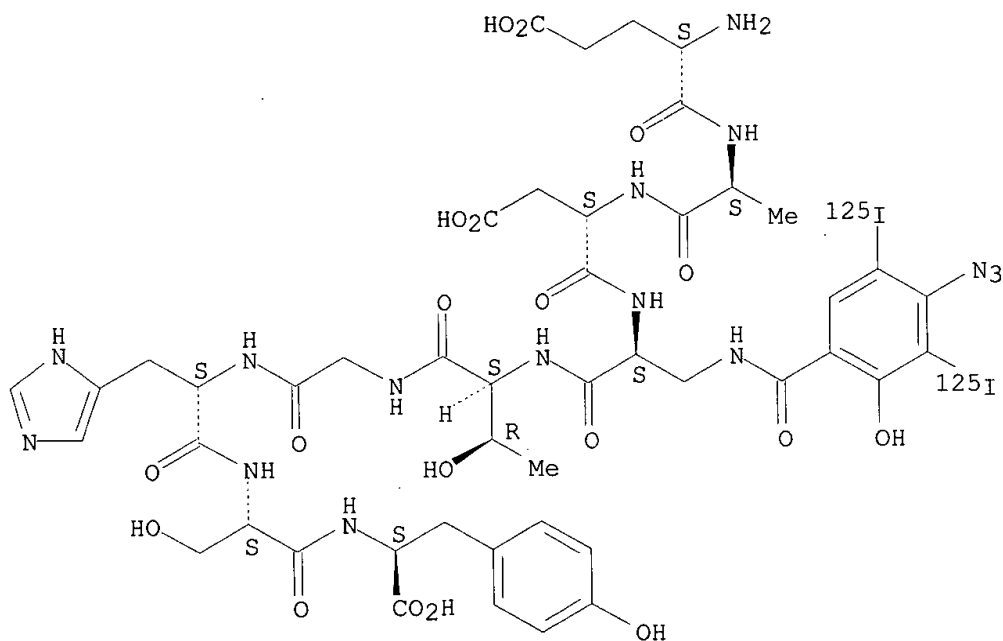


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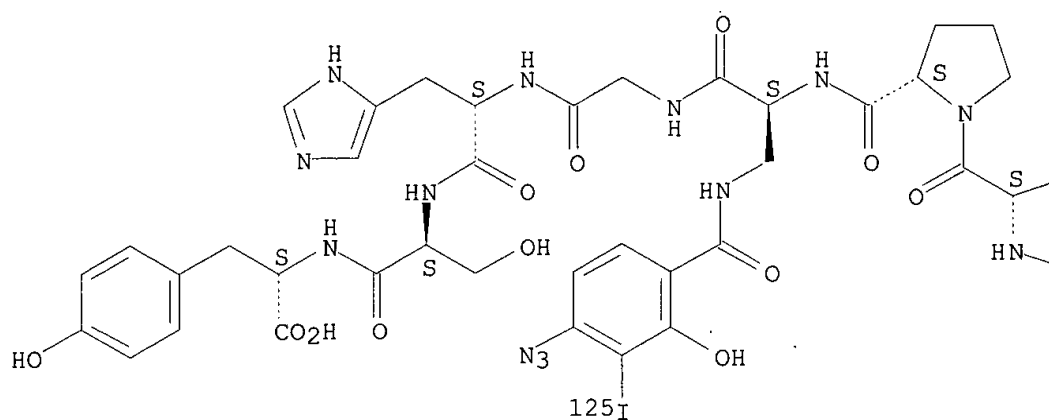
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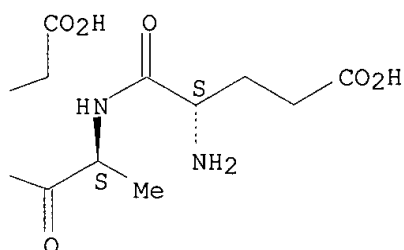
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Absolute stereochemistry.

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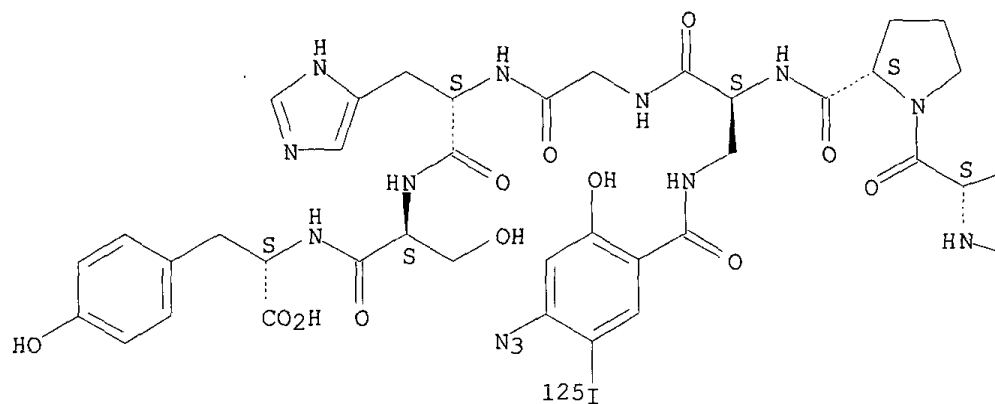


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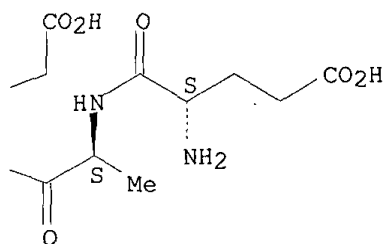
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Absolute stereochemistry.

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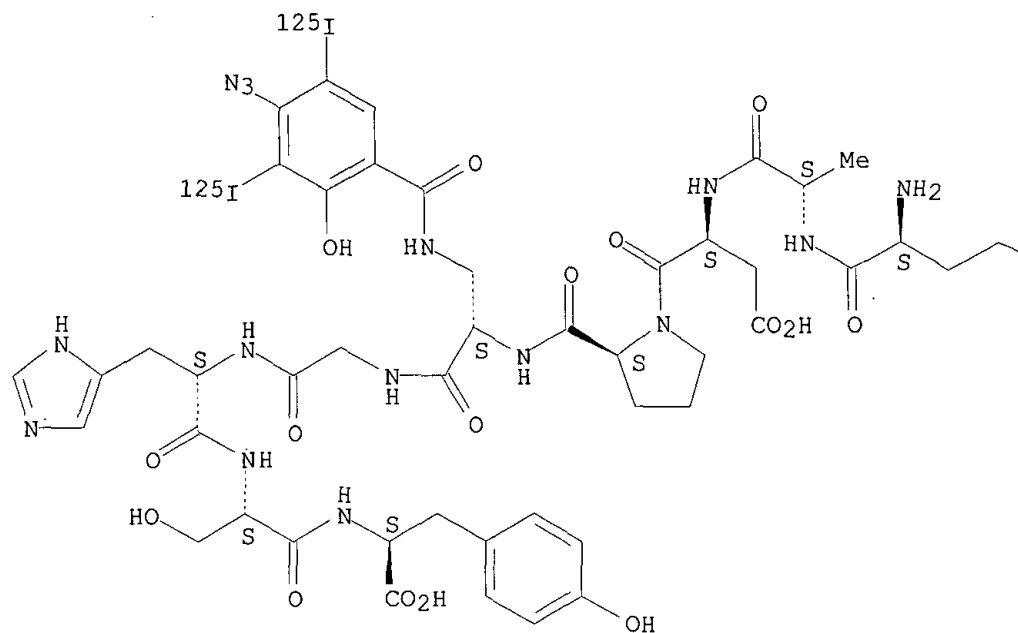
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Absolute stereochemistry.

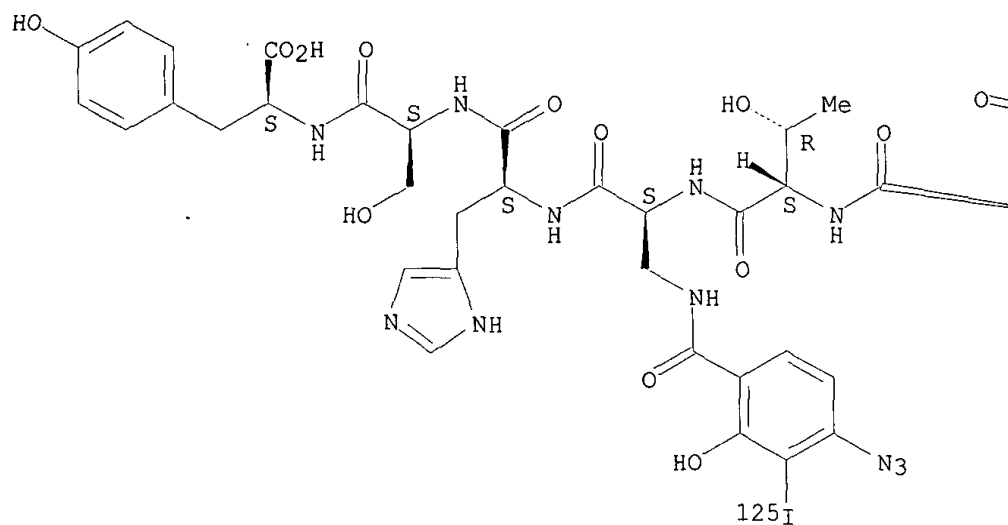


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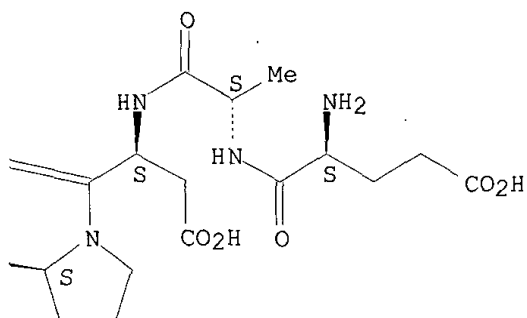
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Absolute stereochemistry.

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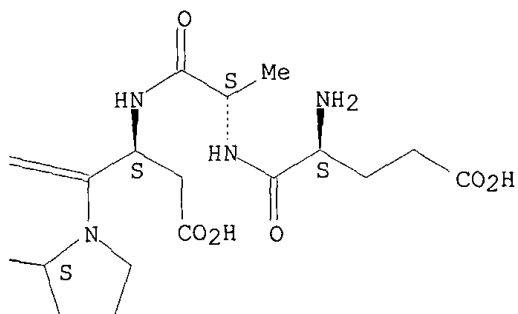
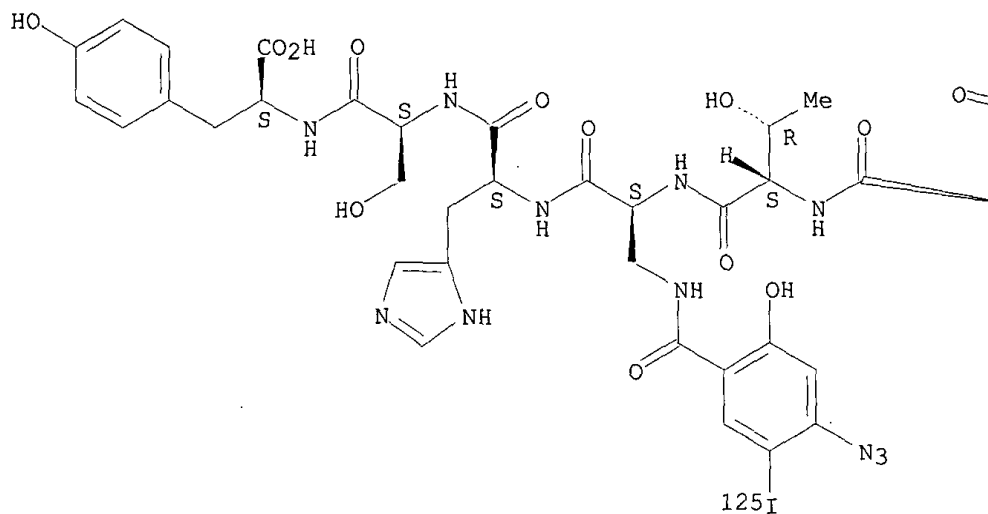
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Absolute stereochemistry.

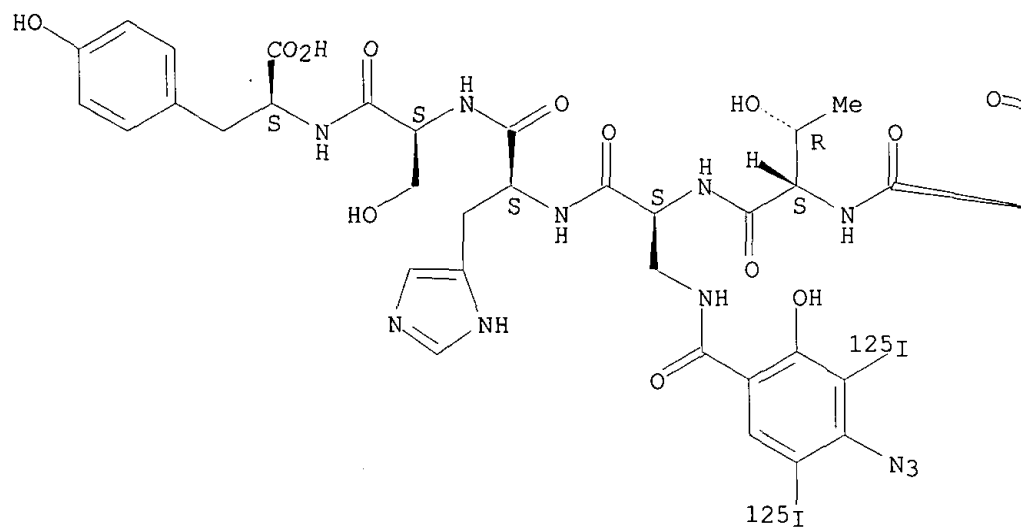


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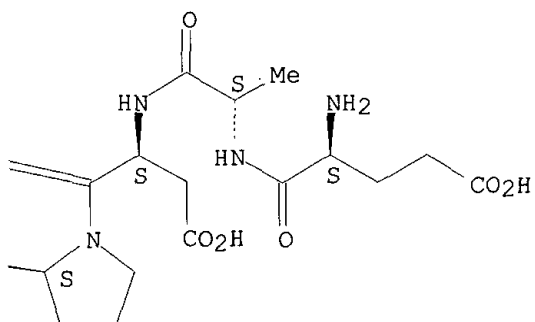
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Absolute stereochemistry.

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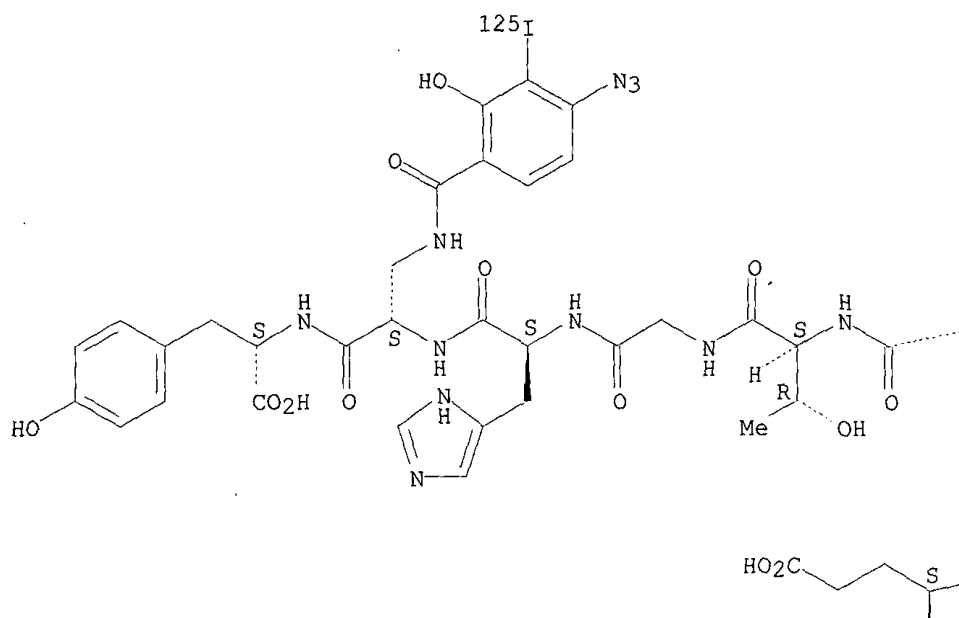
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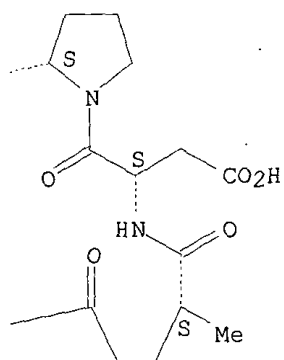
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Absolute stereochemistry.



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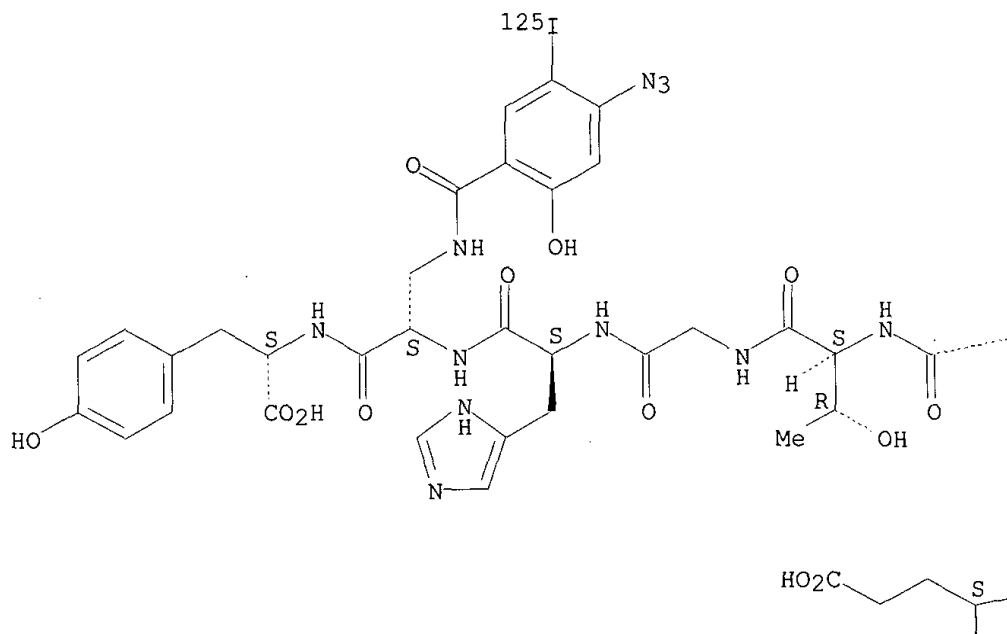
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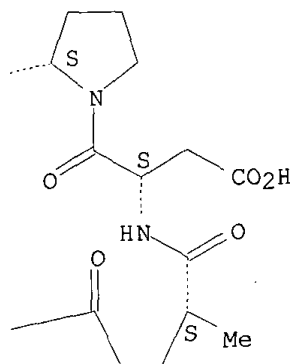
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Absolute stereochemistry.

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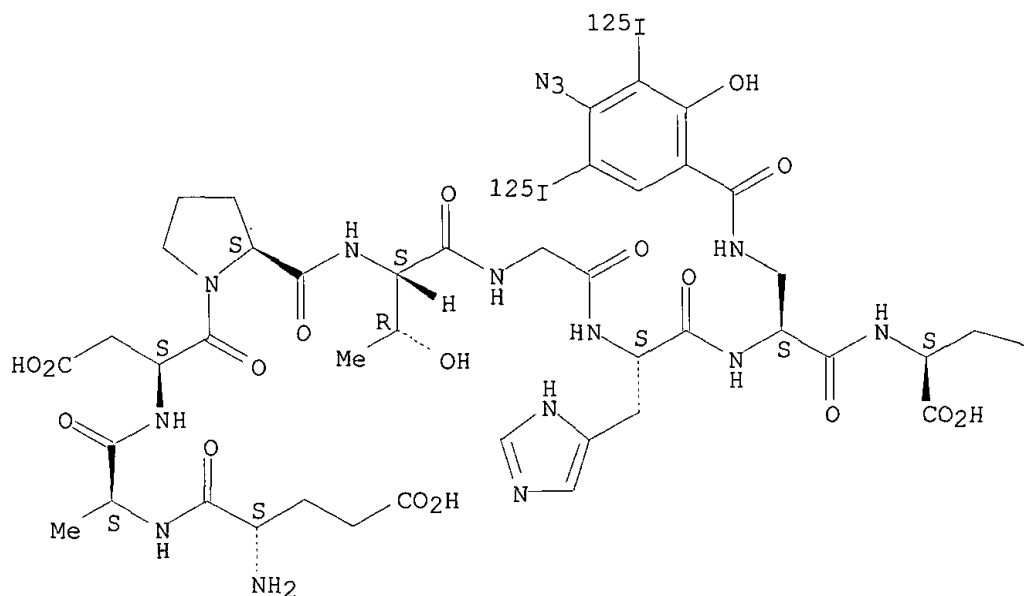
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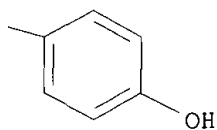
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Absolute stereochemistry.

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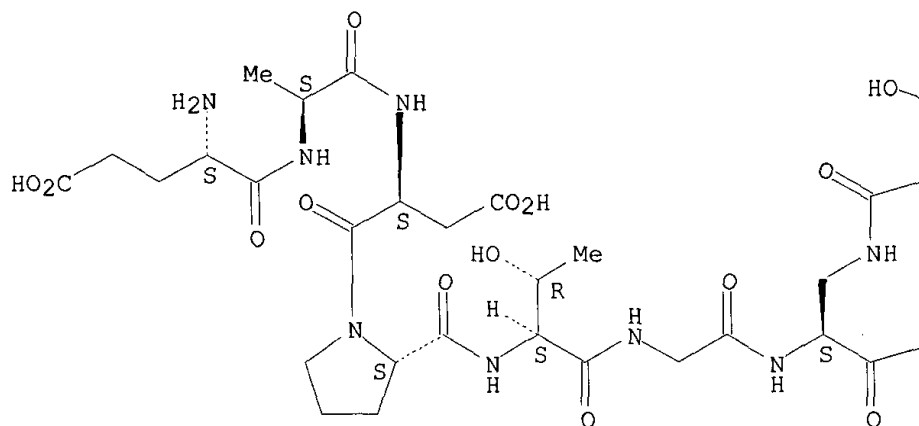


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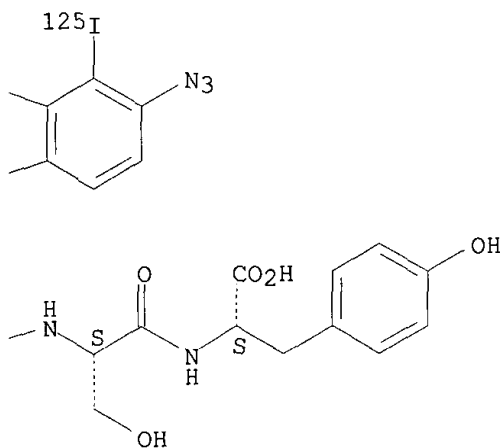
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Absolute stereochemistry.

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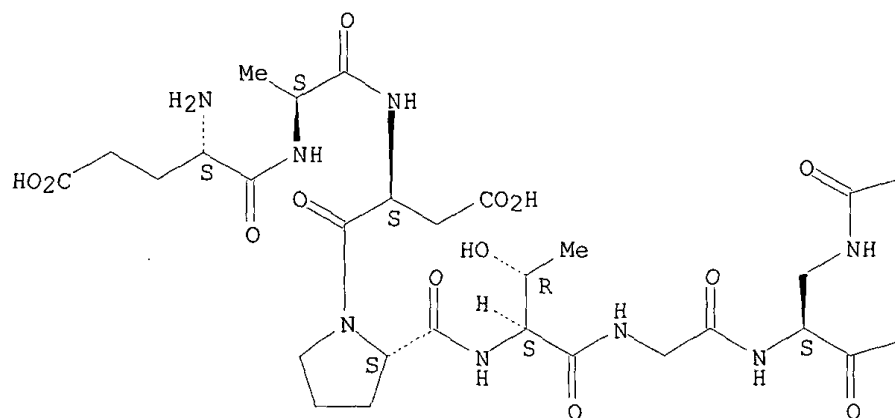


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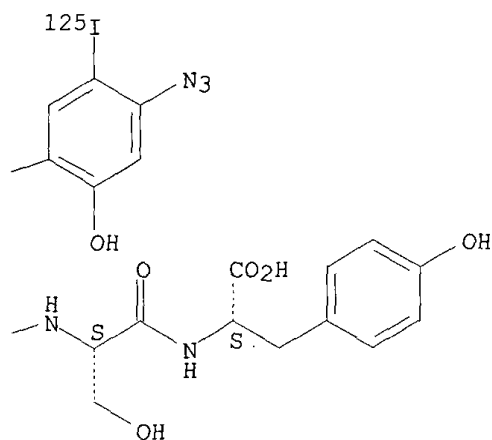
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Absolute stereochemistry.

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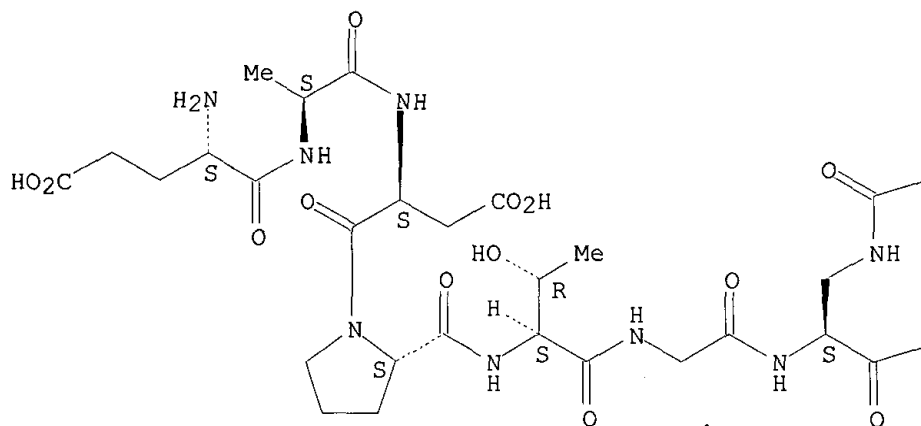


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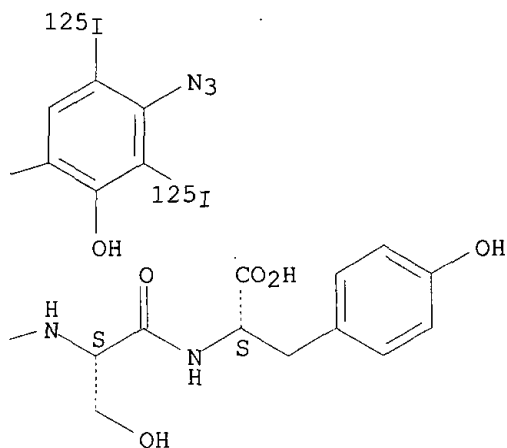
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Absolute stereochemistry.

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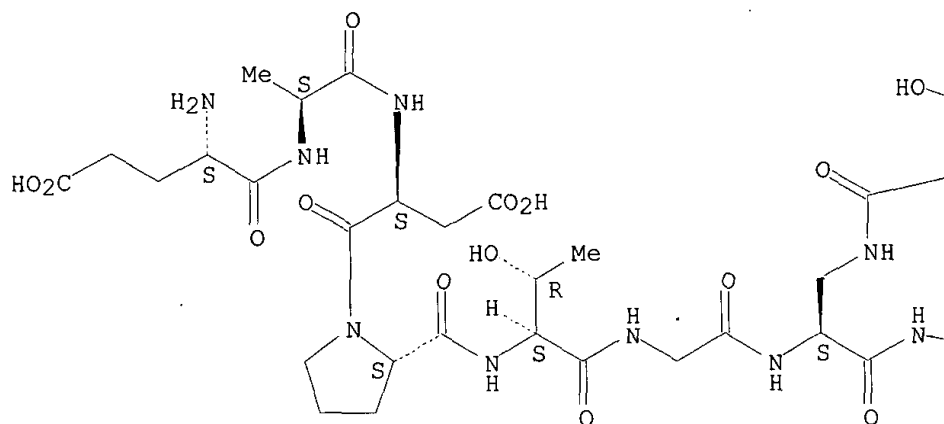


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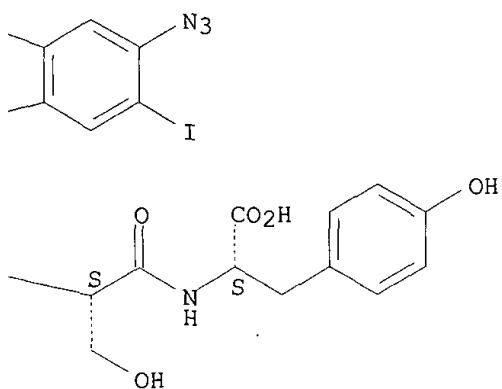
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Absolute stereochemistry.

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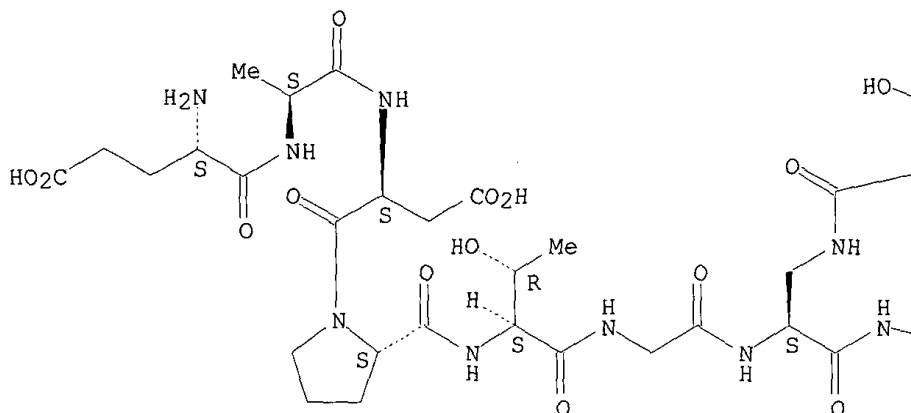


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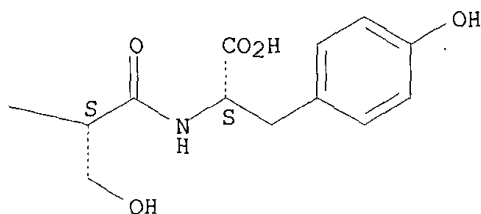
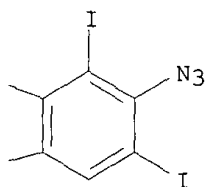
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Absolute stereochemistry.

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IT 187603-36-7P 187603-37-8P 187603-38-9P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of photoreactive peptide derivs. for photoaffinity labeling of
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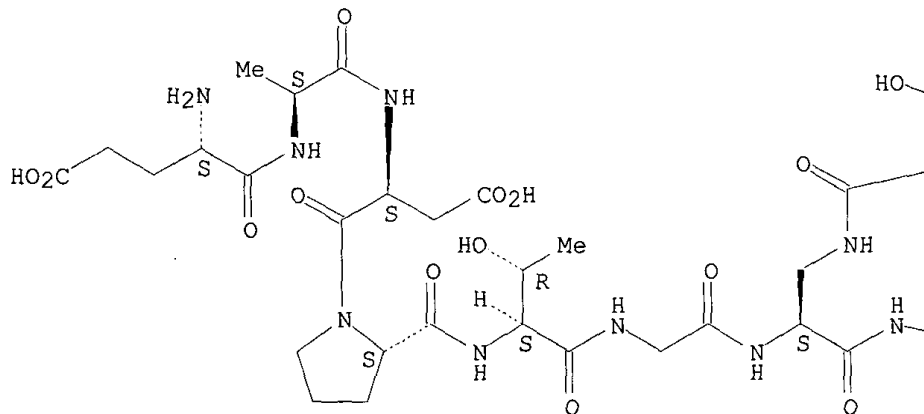
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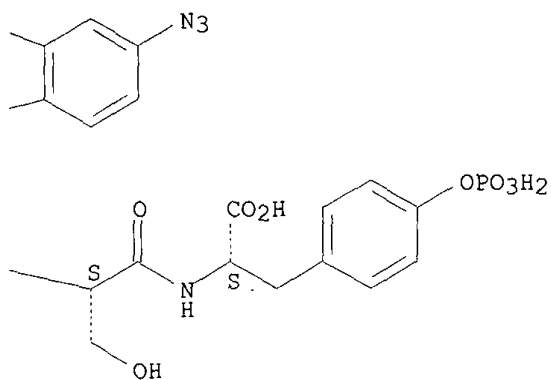
9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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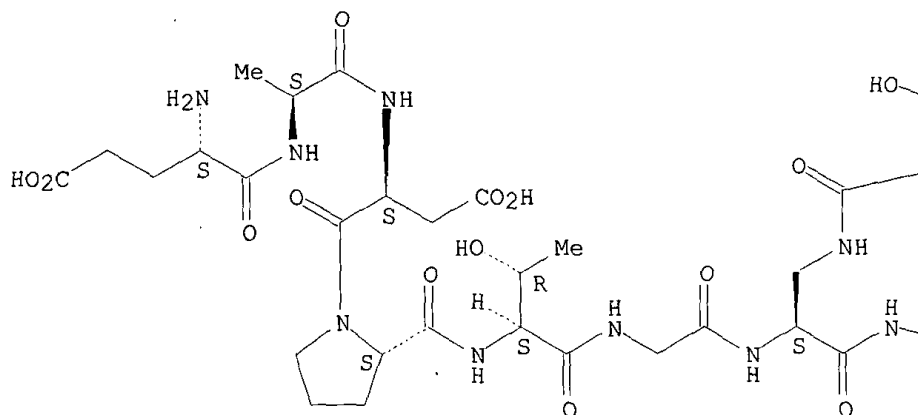


RN 187603-37-8 HCAPLUS

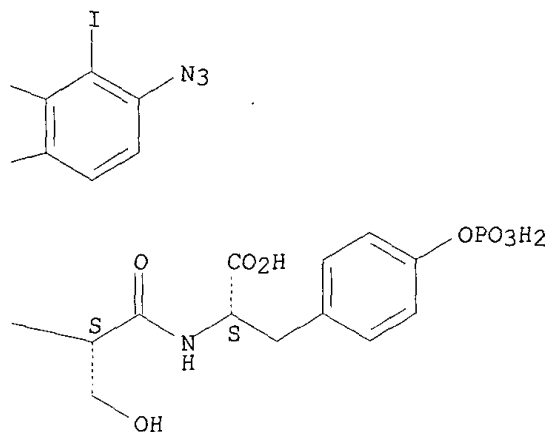
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[(4-azido-2-hydroxy-3-iodobenzoyl)amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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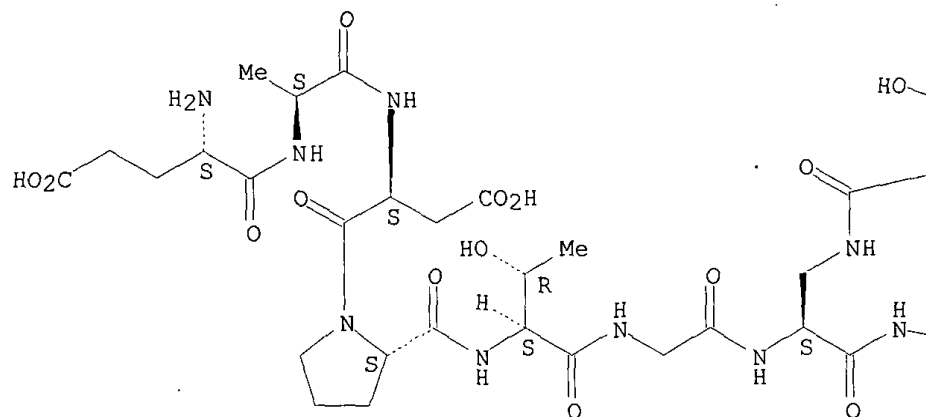


RN 187603-38-9 HCAPLUS

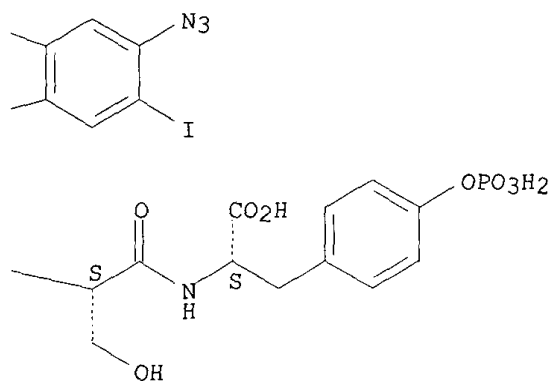
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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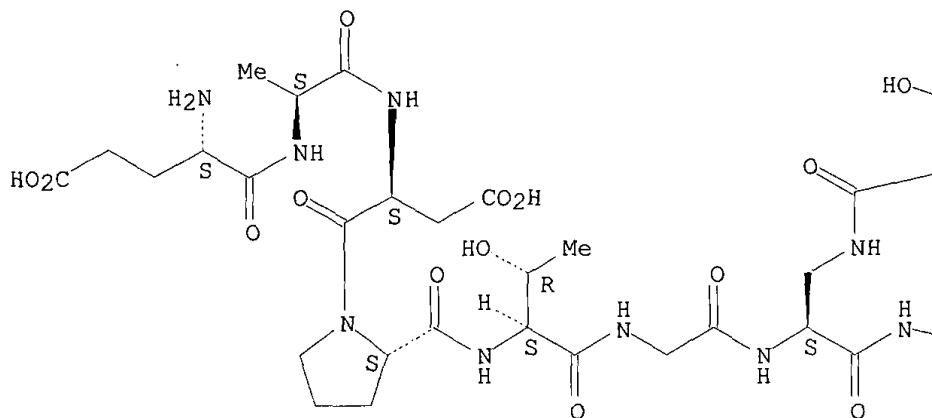


RN 187603-39-0 HCAPLUS

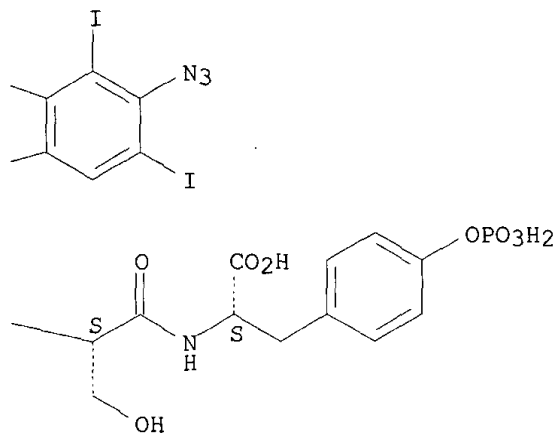
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[(4-azido-2-hydroxy-3,5-diiodobenzoyl)amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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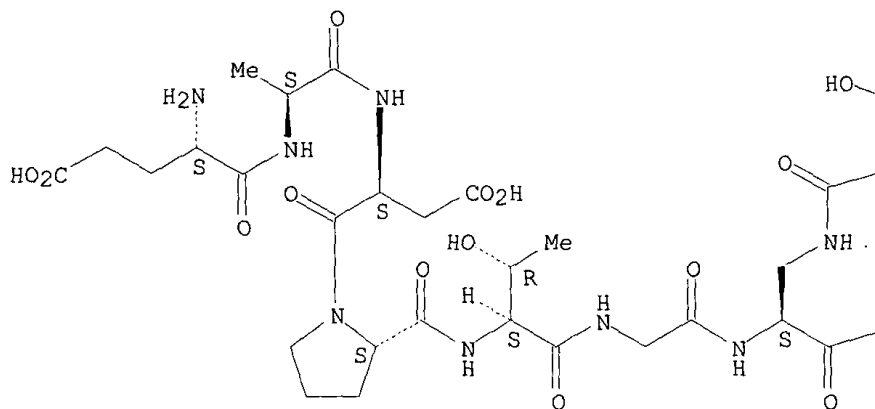


RN 187603-40-3 HCAPLUS

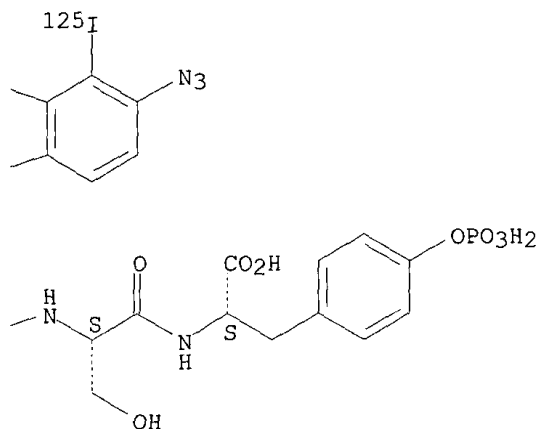
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[[4-azido-2-hydroxy-3-(iodo-125I)benzoyl]amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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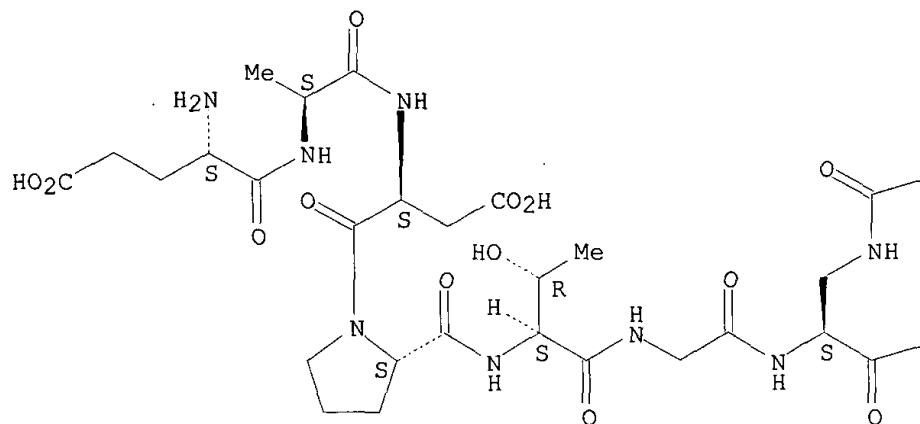


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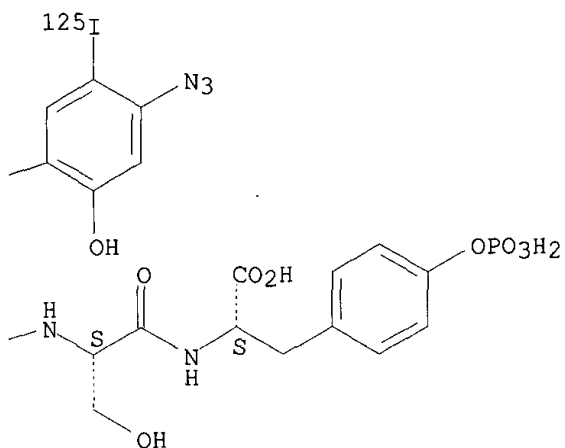
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[[4-azido-2-hydroxy-5-(iodo-125I)benzoyl]amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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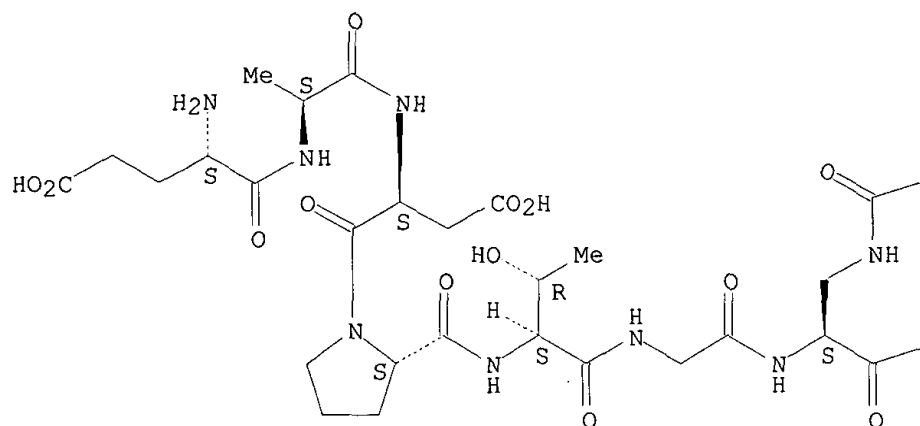


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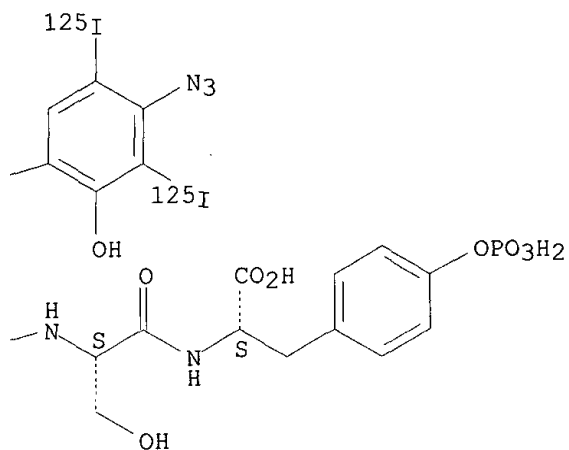
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-3-[[4-azido-2-hydroxy-3,5-di(125I)benzoyl]amino]-L-alanyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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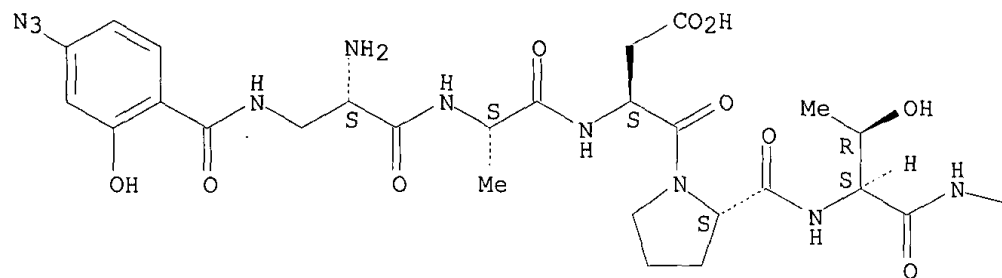


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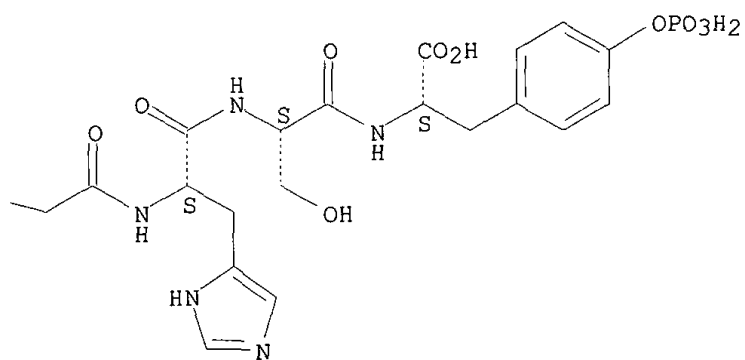
CN L-Tyrosine, 3-[(4-azido-2-hydroxybenzoyl)amino]-L-alanyl-L-alanyl-L-
 .alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-,
 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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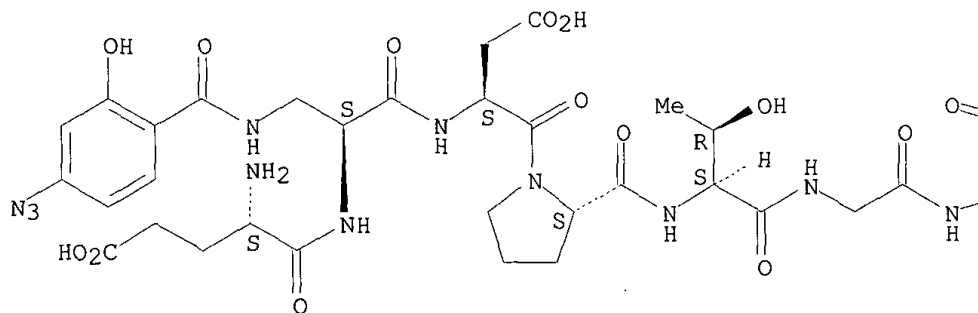


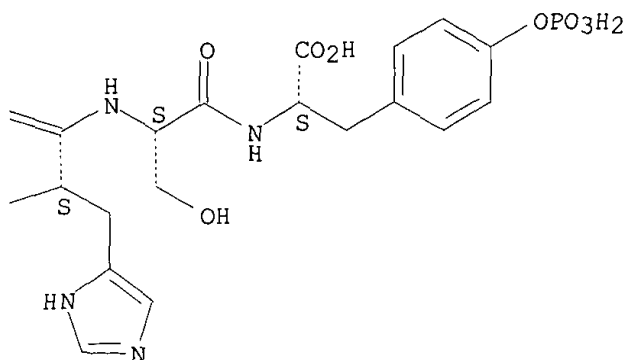
RN 187603-44-7 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-3-[(4-azido-2-hydroxybenzoyl)amino]-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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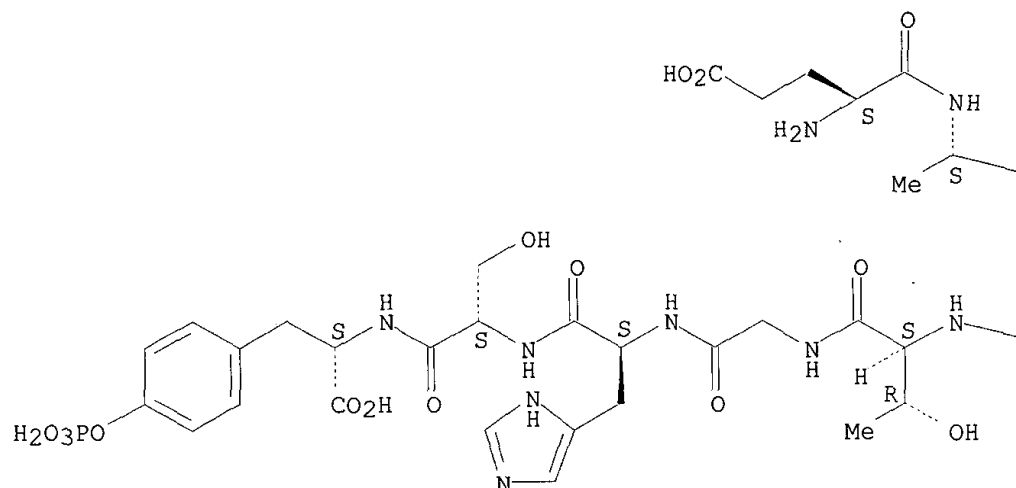


RN 187603-45-8 HCAPLUS

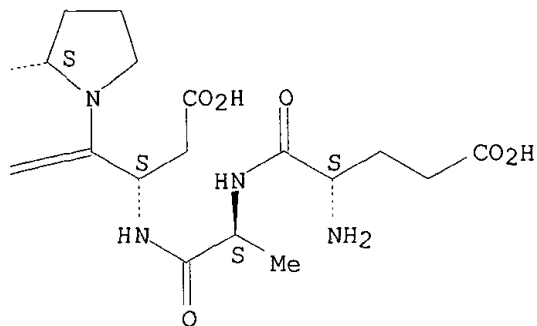
L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-3-[(4-azido-2-hydroxybenzoyl)amino]-L-alanyl-L-threonylglycyl-L-histidyl-L-seryl-,
 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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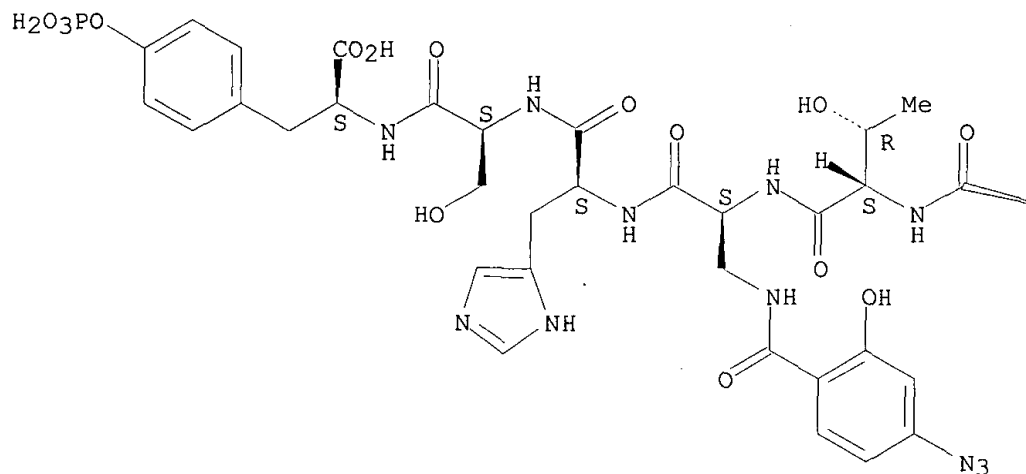


RN 187603-47-0 HCAPLUS

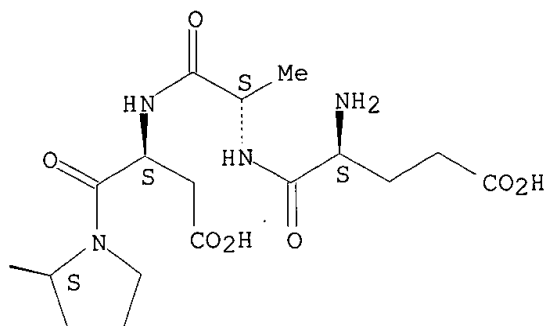
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonyl-3-[(4-azido-2-hydroxybenzoyl)amino]-L-alanyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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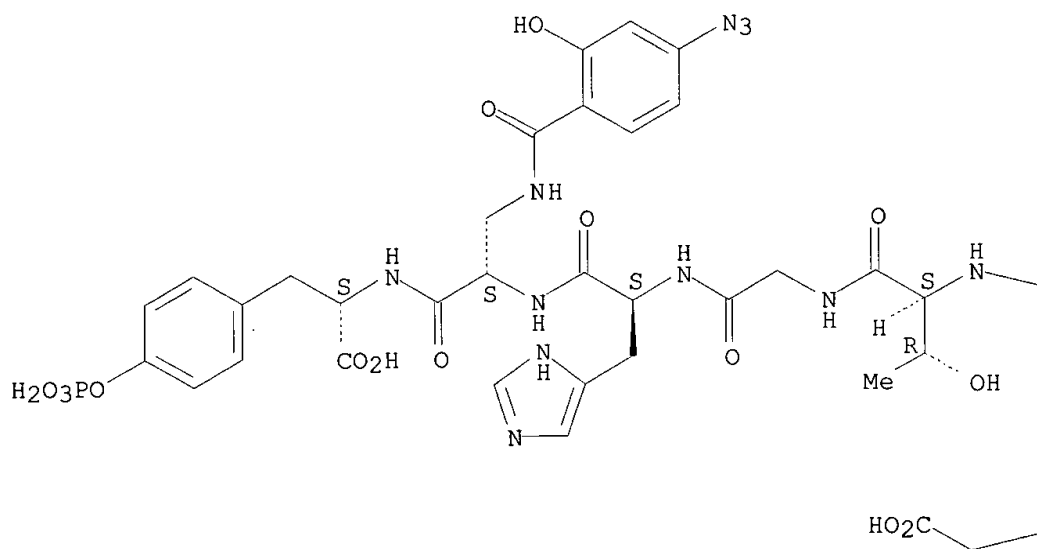


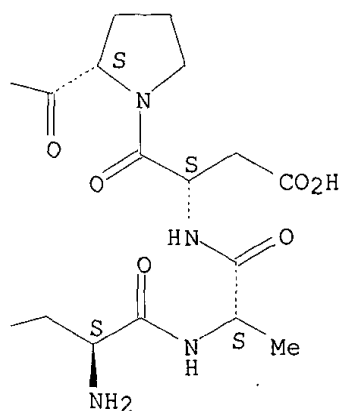
RN 187603-48-1 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-3-[(4-azido-2-hydroxybenzoyl)amino]-L-alanyl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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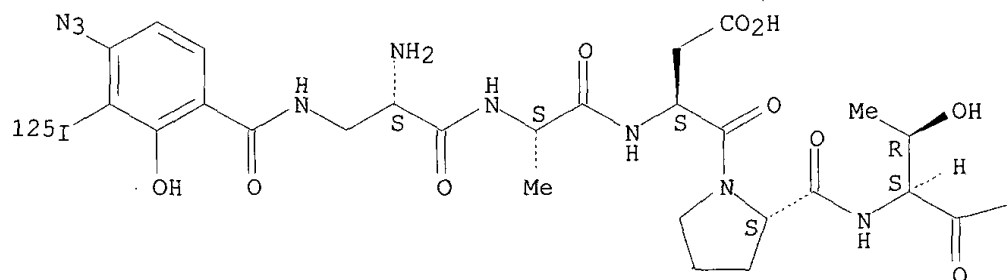




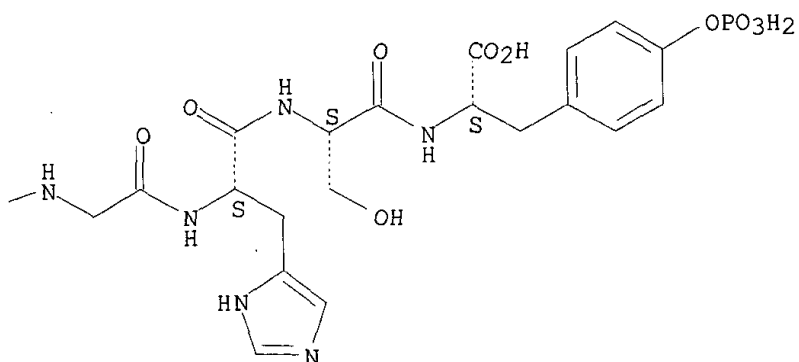
RN 187603-49-2 HCAPLUS

CN L-Tyrosine, 3-[[4-azido-2-hydroxy-3-(iodo-125I)benzoyl]amino]-L-alanyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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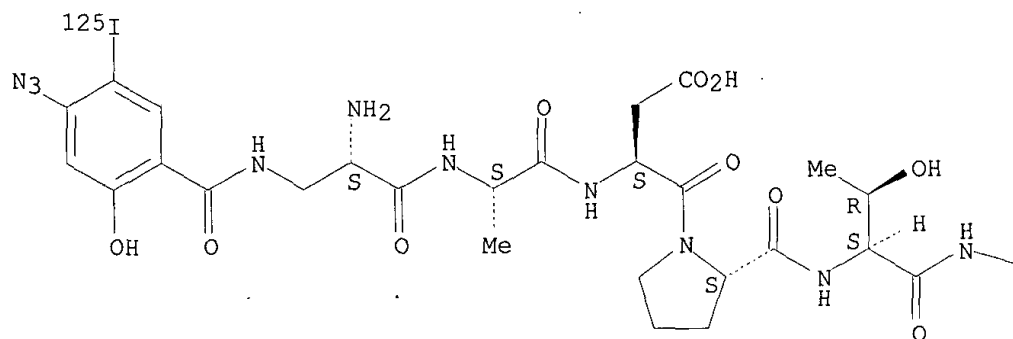


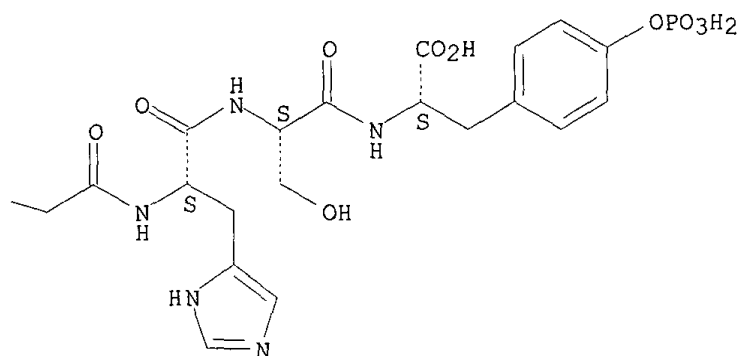
RN 187603-50-5 HCAPLUS

CN L-Tyrosine, 3-[[4-azido-2-hydroxy-5-(iodo-125I)benzoyl]amino]-L-alanyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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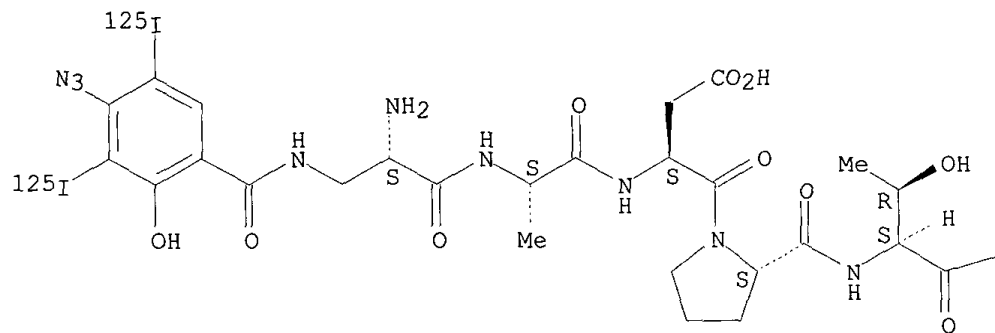


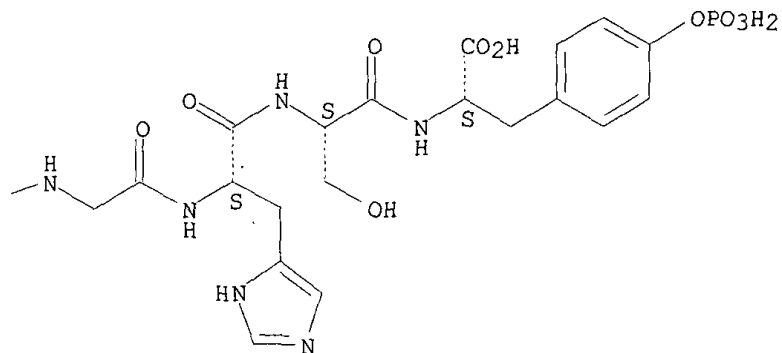


RN 187603-51-6 HCAPLUS

CN L-Tyrosine, 3-[[4-azido-2-hydroxy-3,5-di(iodo-125I)benzoyl]amino]-L-alanyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

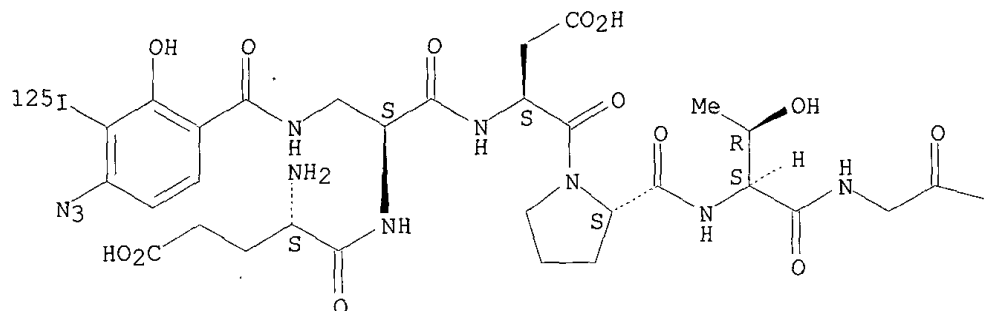




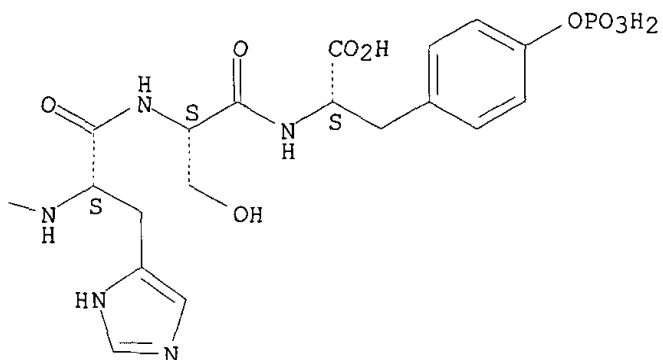
RN 187603-52-7 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-3-[[4-azido-2-hydroxy-3-(iodo-
125I)benzoyl]amino]-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-
L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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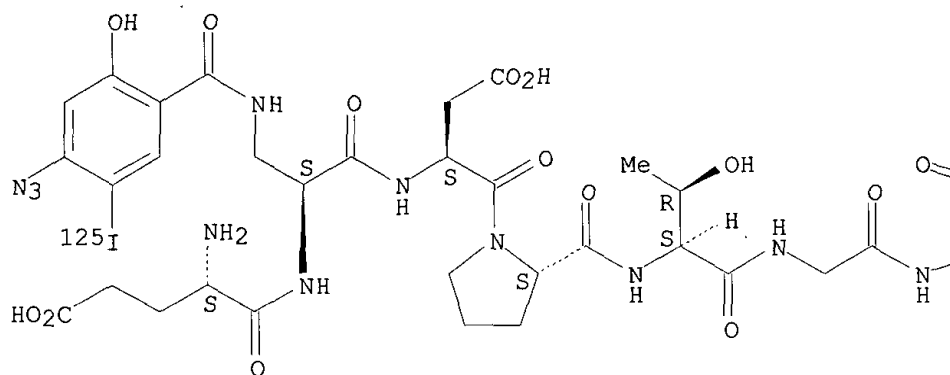


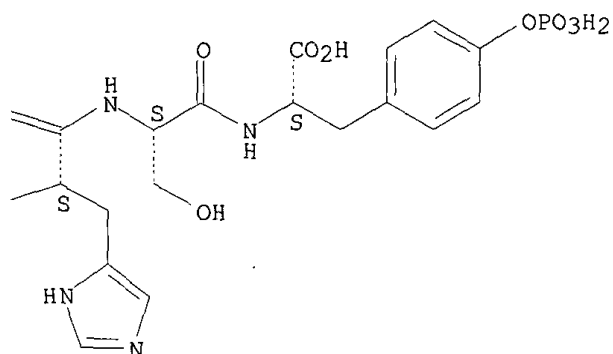
RN 187603-53-8 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-3-[[4-azido-2-hydroxy-5-(iodo-125I)benzoyl]amino]-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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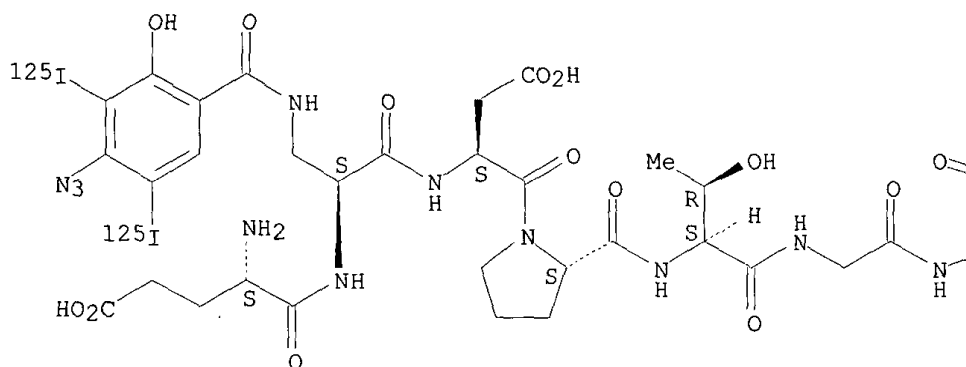


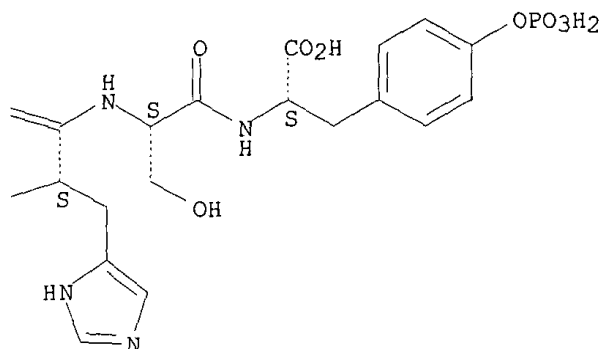


RN 187603-54-9 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-3-[[4-azido-2-hydroxy-3,5-di(iodo-
125I)benzoyl]amino]-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-
L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

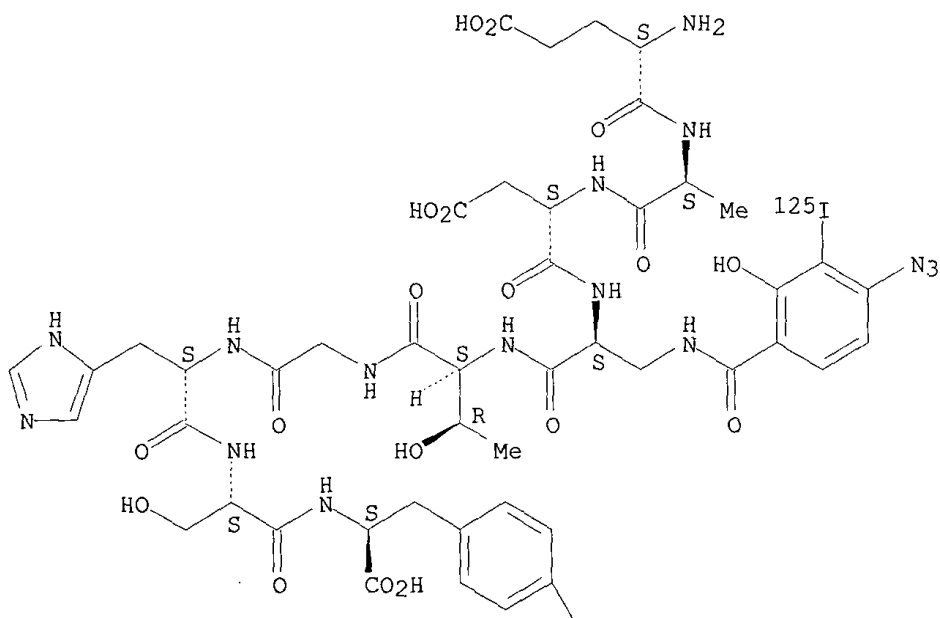




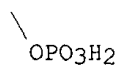
RN 187603-55-0 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-3-[[4-azido-2-hydroxy-3-(iodo-125I)benzoyl]amino]-L-alanyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



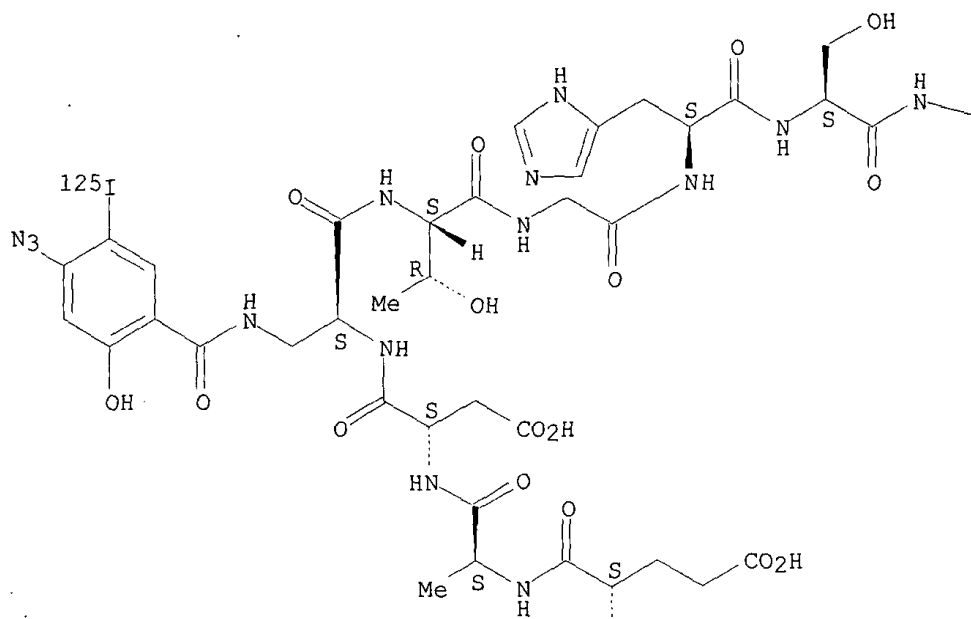
PAGE 2-A



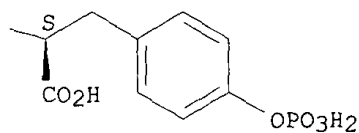
RN 187603-56-1 HCAPLUS
 CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-3-[[4-azido-2-hydroxy-5-(iodo-125I)benzoyl]amino]-L-alanyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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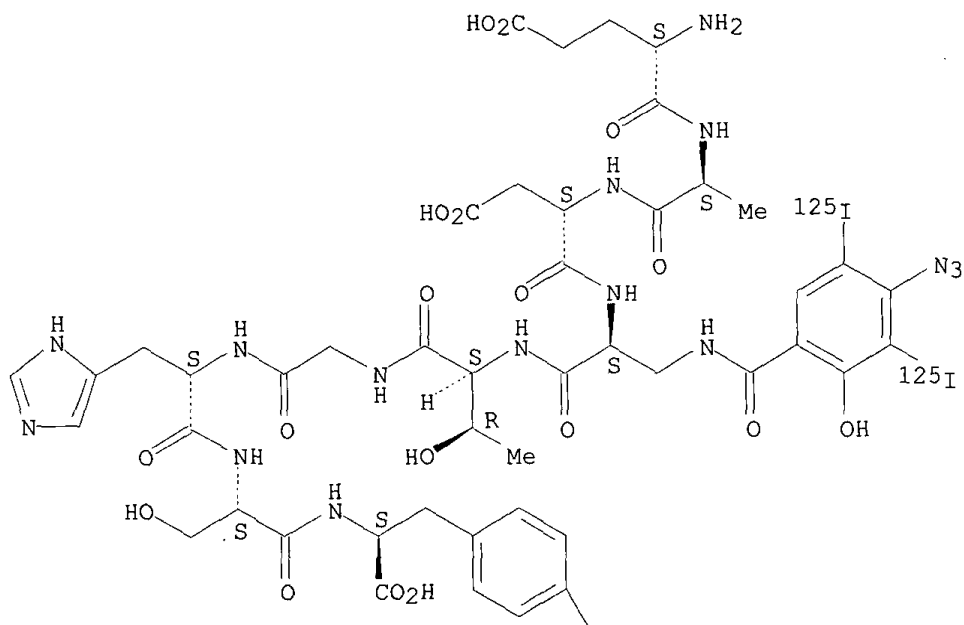


RN 187603-57-2 HCAPLUS

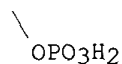
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-3-[[4-azido-2-hydroxy-3,5-di(iodo-125I)benzoyl]amino]-L-alanyl-L-threonylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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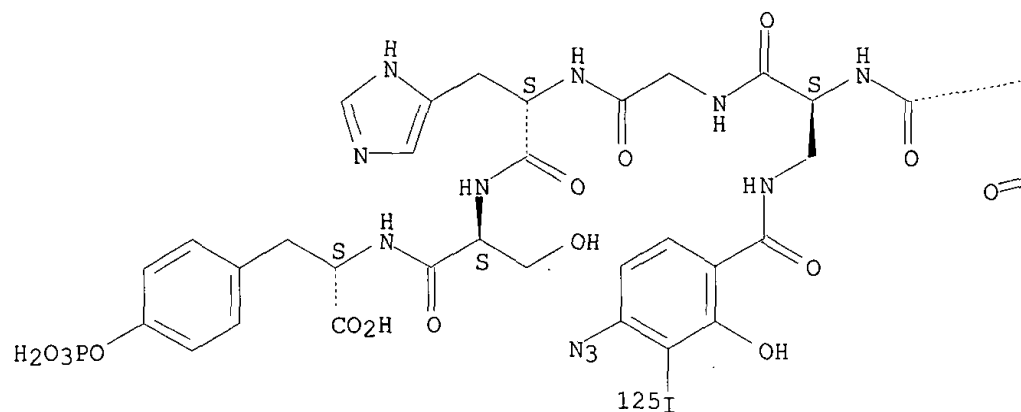


RN 187603-58-3 HCAPLUS

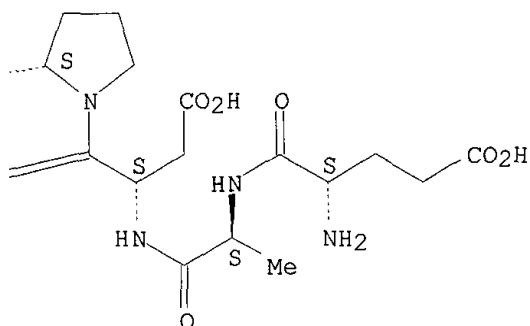
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-3-[[4-azido-2-hydroxy-3-(iodo-125I)benzoyl]amino]-L-alanylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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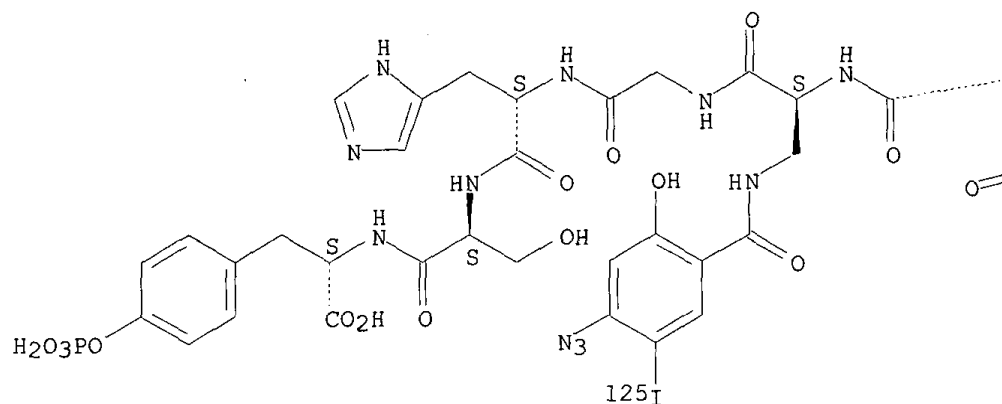


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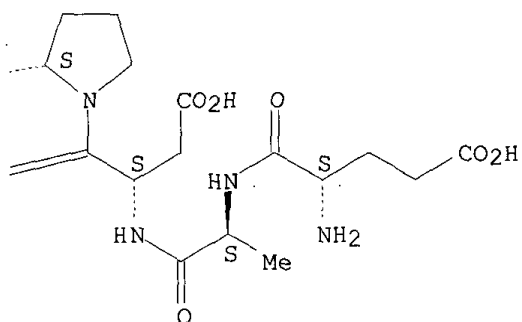
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-3-[[4-azido-2-hydroxy-5-(iodo- ^{125}I)benzoyl]amino]-L-alanylglycyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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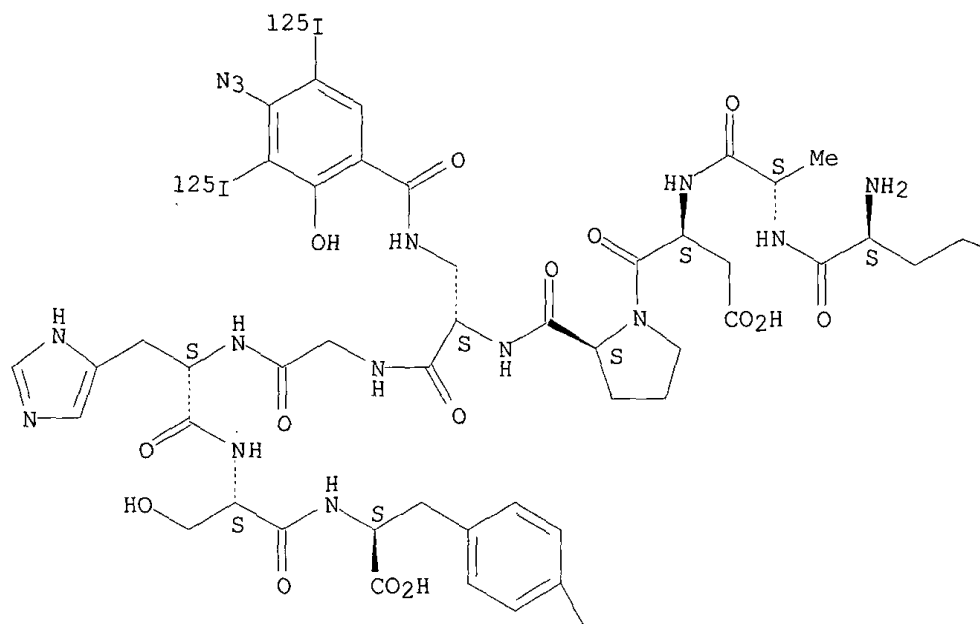


RN 187603-60-7 HCAPLUS

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Absolute stereochemistry.

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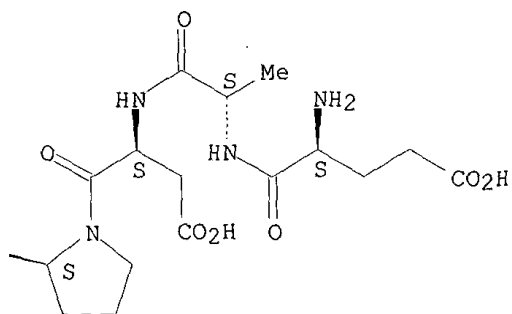
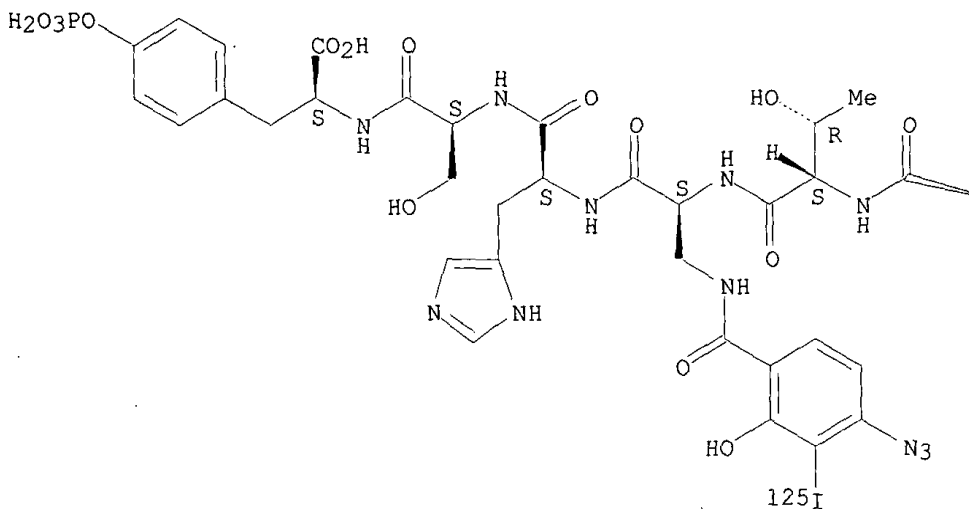
CO₂H

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OPO₃H₂

RN 187603-61-8 HCAPLUS
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Absolute stereochemistry.

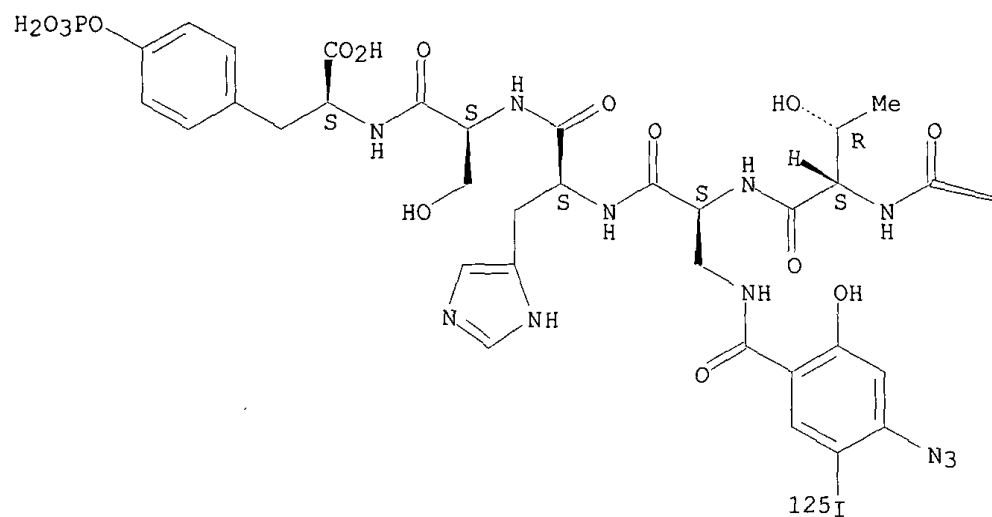


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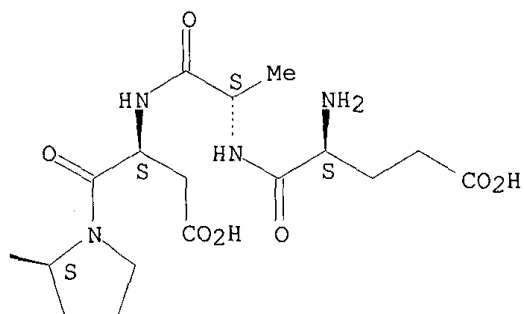
CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonyl-3-[[4-azido-2-hydroxy-5-(iodo-125I)benzoyl]amino]-L-alanyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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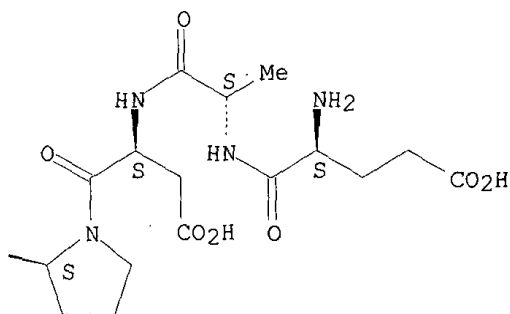
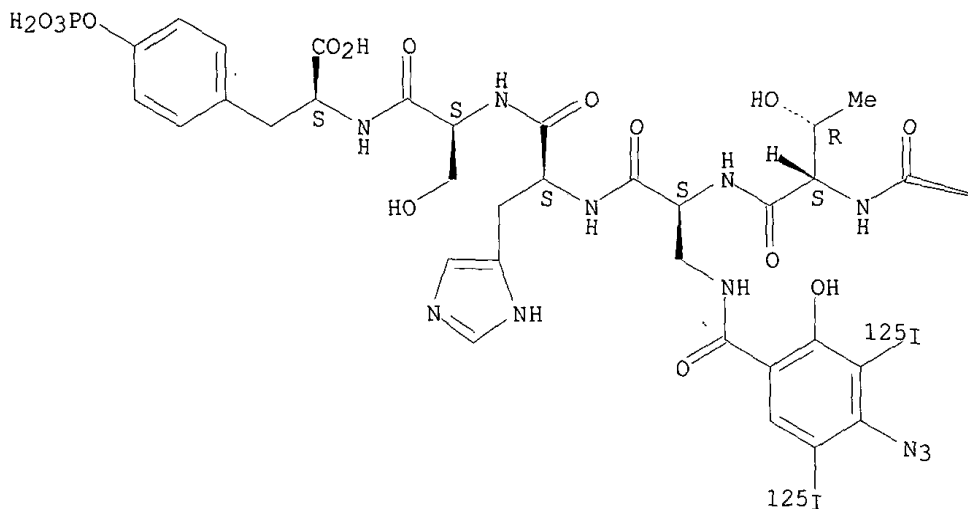
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RN 187603-63-0 HCAPLUS

CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonyl-3-[[4-azido-2-hydroxy-3,5-di(125I)benzoyl]amino]-L-alanyl-L-histidyl-L-seryl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

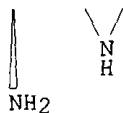


RN 187603-64-1 HCAPLUS

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Absolute stereochemistry.

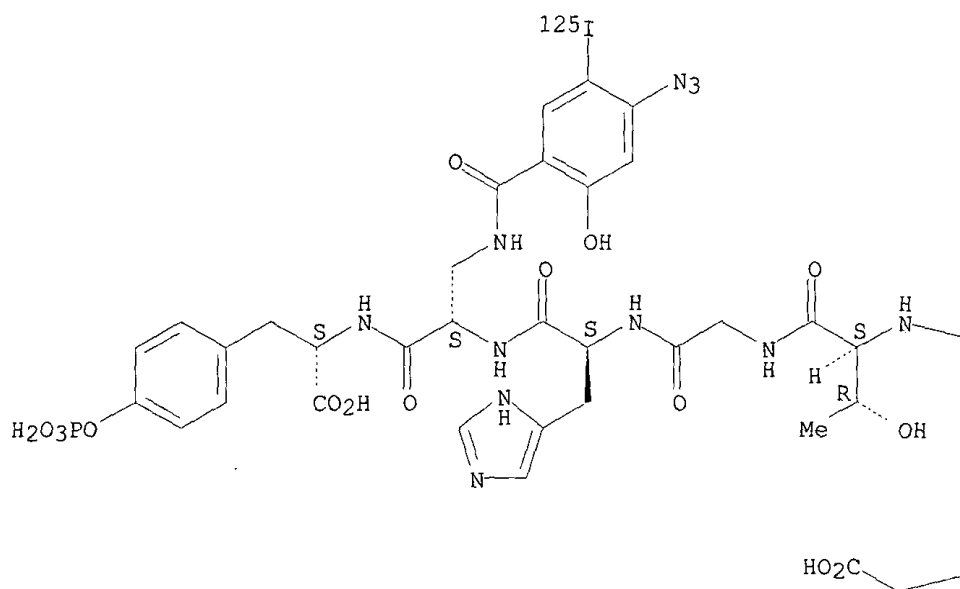
PAGE 2-B



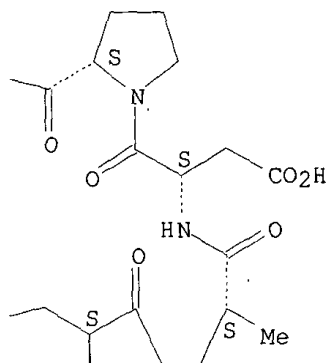
RN 187603-65-2 HCAPLUS
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Absolute stereochemistry.

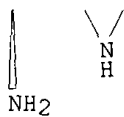
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PAGE 1-B

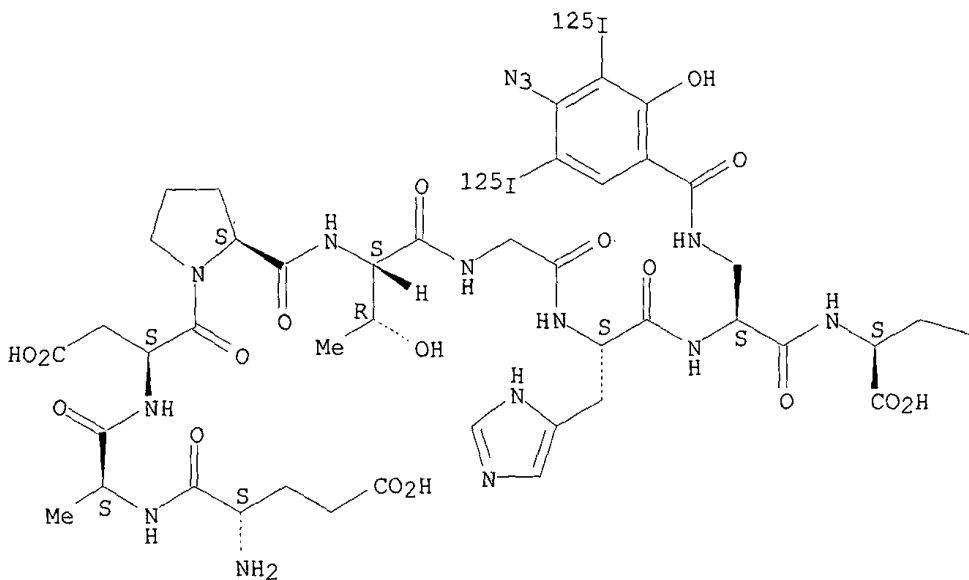


PAGE 2-B

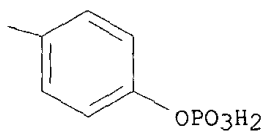


RN 187603-66-3 HCAPLUS
 CN L-Tyrosine, L-.alpha.-glutamyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-threonylglycyl-L-histidyl-3-[[4-azido-2-hydroxy-3,5-di(iodo-125I)benzoyl]amino]-L-alanyl-, 9-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



L31 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:449399 HCAPLUS
DOCUMENT NUMBER: 125:115146
TITLE: Preparation of analogs of the CAAX motif of Ras
protein as inhibitors of farnesyl-protein transferase.
INVENTOR(S): Anthony, Neville J.; Desolms, S. Jane; Graham, Samuel
L.; Stokker, Gerald E.; Wiscount, Catherine M.;
Ciccarone, Terence M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 243 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

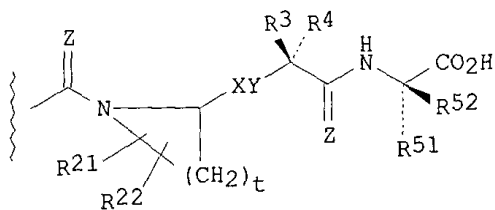
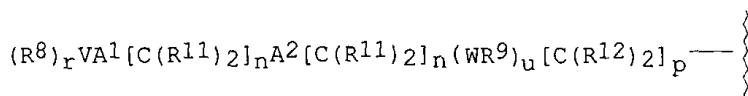
LANGUAGE:

English

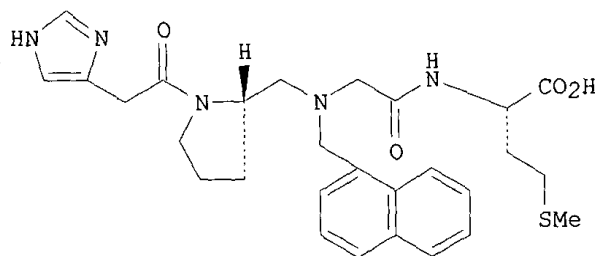
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|--------------|
| WO 9610035 | A1 | 19960404 | WO 1995-US12474 | 19950927 <-- |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, US, US, US, UZ | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5661161 | A | 19970826 | US 1995-527972 | 19950914 <-- |
| AU 9537312 | A1 | 19960419 | AU 1995-37312 | 19950927 <-- |
| AU 701763 | B2 | 19990204 | | |
| EP 783518 | A1 | 19970716 | EP 1995-935199 | 19950927 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 10506900 | T2 | 19980707 | JP 1995-512037 | 19950927 <-- |
| ZA 9508162 | A | 19960424 | ZA 1995-8162 | 19950928 <-- |
| PRIORITY APPLN. INFO.: | | | US 1994-315161 | 19940929 <-- |
| | | | US 1995-399282 | 19950306 <-- |
| | | | US 1995-472077 | 19950606 <-- |
| | | | US 1995-527972 | 19950914 <-- |
| | | | WO 1995-US12474 | 19950927 <-- |
| OTHER SOURCE(S): | | MARPAT 125:115146 | | |
| GI | | | | |



I



II

AB Title compds. [I; R¹¹, R¹² = H, aryl, heterocyclyl, cycloalkyl, alkenyl,

alkynyl, acyl, N3, cyano, NO2, (substituted) alkyl, etc.; R21, R22 = H, (substituted) alkyl, aryl, heterocyclyl, cycloalkyl, alkenyl, acyl, cyano, NO2, N3, amino, etc.; R3, R4, R51, R52 = (oxidized) amino acid side chain, (substituted) alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, etc.; R3R4 = (CH2)s; R51R52 = (CH2)s with 1 C atom optionally replaced by O, S, SO, SO2, NCO, etc.; XY = CONR71, CH2NR72, CH2O, CH:CH, CH2CH2, CH2S, CH2SO, CH2SO2; R71 = H, (substituted) aryl, heterocyclyl, cycloalkyl, alkyl; R72 = R71, CO or SO2 bonded to (substituted) aryl, heterocyclyl, cycloalkyl, alkyl, etc.; R8 = H, aryl, heterocyclyl, cycloalkyl, alkenyl, alkynyl, perfluoroalkyl, F, Cl, Br, N3, amino, (substituted) alkyl, etc.; R9 = H, alkenyl, alkynyl, perfluoroalkyl, F, Cl, Br, cyano, NO2, acyl, (substituted) alkyl, etc.; A1, A2 = bond, CH:CH, C.tplbond.C, CO, O, imino, sulfonylimino, S, SO, SO2, etc.; V = H, heterocyclyl, aryl, alkyl optionally interrupted by O, S, N; W = heterocyclyl; Z = H2, O; n, p = 0-4; r = 0-5; t = 3-5; u = 0, 1], were prepd. Title compds., e.g., (II), inhibited farnesyl-protein transferase with IC50 <10 .mu.M.

IT 179014-32-5P 179014-33-6P

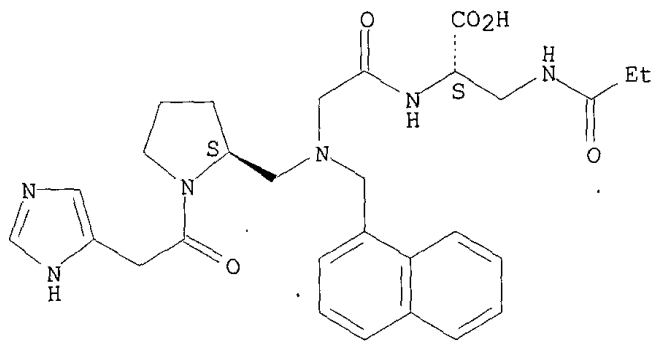
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of analogs of the CAAX motif of Ras protein as inhibitors of farnesyl-protein transferase)

RN 179014-32-5 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

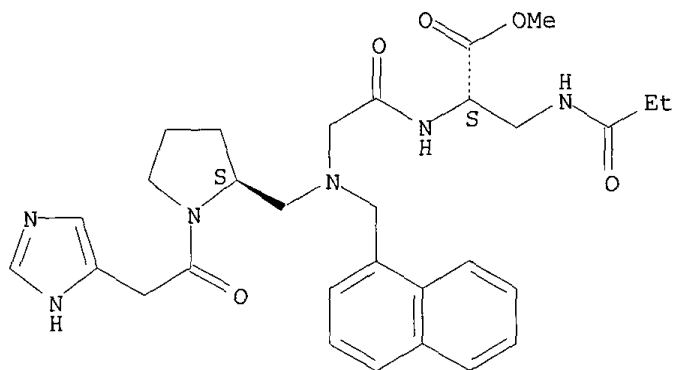
Absolute stereochemistry.



RN 179014-33-6 HCAPLUS

CN L-Alanine, N-[N-[[1-(1H-imidazol-4-ylacetyl)-2-pyrrolidinyl]methyl]-N-(1-naphthalenylmethyl)glycyl]-3-[(1-oxopropyl)amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:701318 HCAPLUS
 DOCUMENT NUMBER: 121:301318
 TITLE: Synthetic, stabilized, three-dimension polypeptides
 INVENTOR(S): Satterthwait, Arnold C., Jr.; Arrhenius, Thomas;
 Chiang, Lin Chang; Cabeza, Edelmina
 PATENT ASSIGNEE(S): Scripps Research Institute, USA
 SOURCE: PCT Int. Appl., 132 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|---------------------|--------------|
| WO 9321206 | A1 | 19931028 | WO 1993-US3032 | 19930331 <-- |
| W: AU, CA, FI, JP, NO | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9339718 | A1 | 19931118 | AU 1993-39718 | 19930331 <-- |
| US 5807979 | A | 19980915 | US 1995-456424 | 19950601 <-- |
| PRIORITY APPLN. INFO.: | | | US 1992-866040 | 19920408 <-- |
| | | | US 1993-33883 | 19930319 <-- |
| | | | US 1988-179160 | 19880408 <-- |
| | | | US 1990-607645 | 19901029 <-- |
| | | | US 1991-746064 | 19910812 <-- |
| | | | WO 1993-US3032 | 19930331 <-- |
| | | | US 1994-224059 | 19940407 <-- |
| OTHER SOURCE(S): | | | CASREACT 121:301318 | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Synthesis of three-dimensional stabilized peptides which mimic the three-dimensional configuration of active site of a natural, biol. active protein is carried out by (1) noting the three-dimensional configuration of the active site of a known biol. active protein, (2) noting the amino acid sequence and the hydrogen bonds existing between amino acids and that hydrogen bonds are capable of maintaining the three-dimensional

configuration of the active site, and (3) producing a synthetic three-dimensional peptide to mimic the structure of the active site. The synthetic peptide is synthesized so as to have the same or a similar amino acid sequence to the amino acid sequence of the active site of the biol. active polypeptide but with the stabilizing hydrogen bonds being replaced by a bridging divalent radical selected from the group consisting of aminomethane and aminoethane acetamidinium (N)CMe:N(H⁺)CH₂(N), (N)CMe:N(H⁺)CH₂CH₂(N) (class I hydrogen bond mimics), and carboxybutanal hydrazone (N)N:CH(CH₂)₃(CO) (class II hydrogen bond mimic). Said peptides are represented by general cyclic peptide formulas (I; R₁, R₂ = H, C1-6 alkyl; R₃ = H, C1-6 alkyl, chain of amino acids contg. 1-2,000 amino acids; aa = amino acid; n = 1-2,000; R₄ = any atom or mol. group of atoms with the required electron configuration; m = 0-6) and [II; R₅ = C1-6 alkoxy, PhO, naphthyl, benzoxy, NH₂, an amino acid sequence contg. 1-2,000 amino acids; aa = amino acid; n = 1-2,000; m = integer, e.g. 2; X = optionally present and if present is selected from the group consisting of CH₂, NH, :CH, and :NH with double bond to CHR; R₆ = optionally present and if present is selected from the group consisting of H, C1-6 alkyl, (CH₂)₁NH₂ (wherein 1 = 1-6) optionally connected to an amino acid chain contg. 1-2,000 amino acids]. The hydrogen bond mimic (class I) of the cyclic peptide I is formed by intramol. reaction of the thioimide group [generated by treating the corresponding thioamide R₁C(S)NR₂CHR₃(CO) with MeI] of a peptide (III) with the primary NH₂ group. The cyclic peptide II are prepd. by intramol. cyclocondensation of the hydrazide group of a peptide (IV) with the di-Me acetal functional group, forming the other type of the hydrogen bond mimics (class II). Thus, 5 conformationally restricted HIV peptides with the hydrogen bond mimic (class II), e.g. cyclic peptide II [(aa)_n = S-I-G-P-G-R-A-F-G, m = 2, X = bond, R₆ = H, R₅ = Cys-NH₂] (V), which is related to the V3 loop of the HIV gp120 protein identified as a neutralizing epitope, were prepd. by the solid phase method. V bound to 3 HIV-binding murine monoclonal antibodies, at least one of which protected monkey against HIV, and reacted pos. using ELISA with sera from a patient with AIDS. HIV peptide II [(aa)_n = S-I-S-I-G-P-G-R-A-F-Y-T-G, m = 2, X = bond, R = H, R = Cys-NH] was used to isolate human Fabs from combinatorial libraries by panning and these 5 peptides are potential synthetic vaccines for protection against AIDS. Conformationally restrained malaria peptides corresponding to neutralizing epitopes on various stages of Plasmodium falciparum malaria were also prepd. and are useful as a multistage vaccine. Also prepd. were epidermal growth factor analogs contg. carboxybutanal hydrazone linkage (class II) as hydrogen bond mimic.

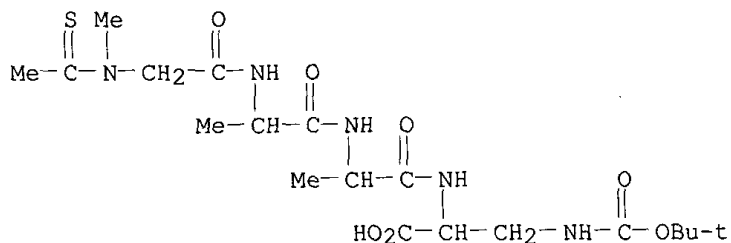
IT 158966-04-2DP, leucine-modified resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn., methylation with Me iodide, deprotection and resin-cleavage-cyclization of)

RN 158966-04-2 HCAPLUS

CN Alanine, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-N-[N-[N-[N-methyl-N-(1-thioxyethyl)glycyl]-L-alanyl]-L-alanyl]- (9CI) (CA INDEX NAME)



L31 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:152405 HCAPLUS
 DOCUMENT NUMBER: 116:152405
 TITLE: Preparation of somatostatin analogs
 INVENTOR(S): Schally, Andrew V.; Janaky, Tamas; Cai, Ren Zhi
 PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA
 SOURCE: Eur. Pat. Appl., 28 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 450480 | A2 | 19911009 | EP 1991-104845 | 19910327 <-- |
| EP 450480 | A3 | 19911218 | | |
| EP 450480 | B1 | 19950621 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| ES 2075244 | T3 | 19951001 | ES 1991-104845 | 19910327 <-- |
| CA 2039880 | AA | 19911007 | CA 1991-2039880 | 19910405 <-- |
| AU 9174105 | A1 | 19911010 | AU 1991-74105 | 19910405 <-- |
| AU 638118 | B2 | 19930617 | | |
| HU 59165 | A2 | 19920428 | HU 1991-1117 | 19910405 <-- |
| JP 06041194 | A2 | 19940215 | JP 1991-72935 | 19910405 <-- |
| | | | US 1990-505501 | 19900406 <-- |

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 116:152405

GI For diagram(s), see printed CA Issue.

AB The title compds. I [Q = H, L- or D-Mel, Mel-Mel, cyclopropanealkanoic acid residue, etc.; Mel = 4-[bis(2-chloroethyl)amino]phenylalanine residue; R1 = L- or D-Phe, D-Trp, L- or D-Mel; R3 = Mel, Tyr, Phe; R6 = Thr, Val; R8 = Thr, Trp, Mel] and II [R1 = L- or D-Phe, L- or D-Try; R3 = Phe, Trp; R6 same as defined above; R8 = Thr, Trp; A = -HNCH2(CH2)mCH(NH)(CH2)nCO-; m, n = 0, 1; Q1 = cytotoxic moiety] and their pharmaceutical acceptable salts were prepd. Successive coupling of BOC-Thr(Bzl)-OH, BOC-Cys(MBzl)-OH, BOC-Val-OH, BOC-Lys[Z(2-Cl)]-OH, BOC-D-Trp-OH, BOC-Tyr[Z(2-Br)]-OH, BOC-Cys(MBzl)-OH, and BOC-Mel-OH [Bzl = benzyl, MBzl = methylbenzyl] to a benzhydrylamine resin, cleavage of the resulting peptide from the resin, oxidn., and deprotection gave I [Q = H, R1 = Mel, R3 = R8 = Tyr, R6 = Val] (III). In an in vitro study using dispersed rat pituitary cell superfusion system the affinity consts. of III to rat cortex and prostate tumor cell membranes were 13.355 and 1.378 .times. 10⁹M⁻¹, resp., compared with 15.795 and 1.378 .times. 10⁹M⁻¹ for somatostatin (1-14).

IT 139668-82-9DP, benzhydrylamine resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)

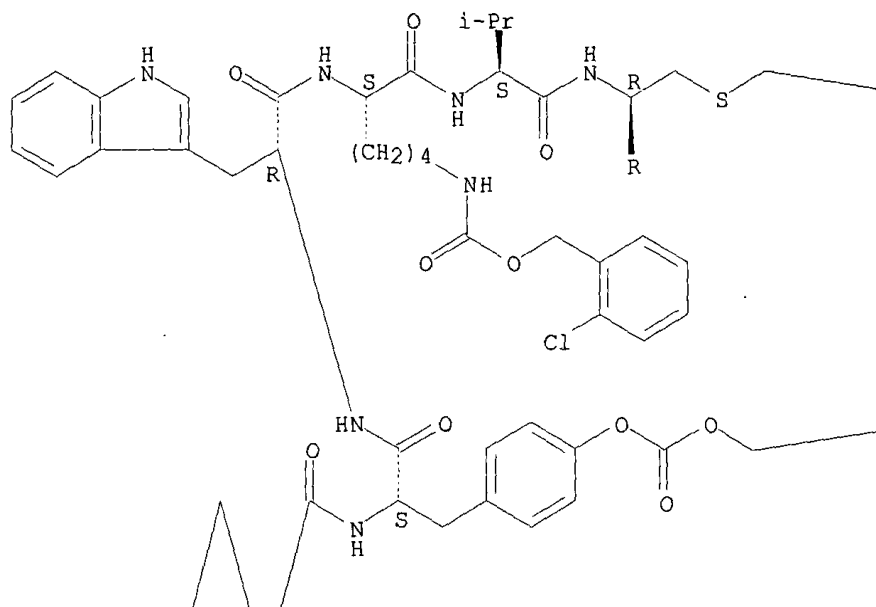
(prepn. of, as intermediate for somatostatin analogs)

RN 139668-82-9 HCAPLUS

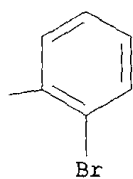
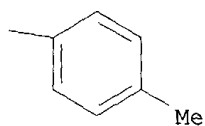
CN L-Threoninamide, N-[(1,1-dimethylethoxy)carbonyl]-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanyl-D-phenylalanyl-S-[(4-methylphenyl)methyl]-L-cysteinyl-O-[(2-bromophenyl)methoxy]carbonyl]-L-tyrosyl-D-tryptophyl-N6-[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-L-valyl-S-[(4-methylphenyl)methyl]-L-cysteinyl-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

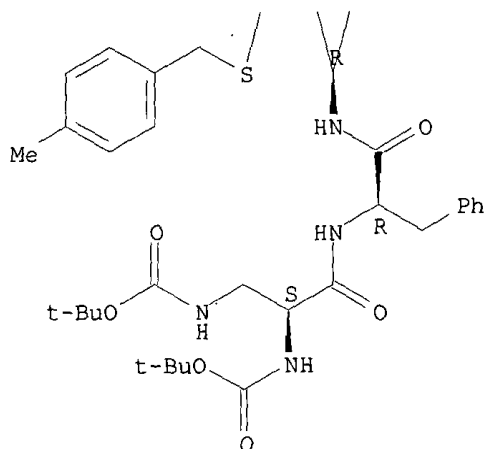
PAGE 1-A



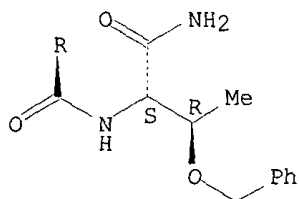
PAGE 1-B



PAGE 2-A



PAGE 3-A



L31 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:472235 HCAPLUS
 DOCUMENT NUMBER: 115:72235
 TITLE: Preparation of aspartic acid-containing pentapeptides
 as antiherpes agents
 INVENTOR(S): Adams, Julian; Beaulieu, Pierre Louis; Deziel, Robert;
 DiMaio, John; Grenier, Louis; Lavallee, Pierre; Moss,
 Neil
 PATENT ASSIGNEE(S): Bio-Mega Inc., Can.
 SOURCE: Eur. Pat. Appl., 19 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 411334 | A1 | 19910206 | EP 1990-112646 | 19900703 <-- |
| EP 411334 | B1 | 19950222 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| CA 2019005 | AA | 19911214 | CA 1990-2019005 | 19900614 |
| IL 94980 | A1 | 19950315 | IL 1990-94980 | 19900705 <-- |
| JP 03215497 | A2 | 19910920 | JP 1990-179373 | 19900706 <-- |
| JP 2877909 | B2 | 19990405 | | |

| | | | | |
|------------------------|----|------------------|-----------------|--------------|
| AU 643636 | B2 | 19931118 | AU 1990-58775 | 19900706 <-- |
| AU 9058775 | A1 | 19910110 | | |
| US 5502036 | A | 19960326 | US 1994-208168 | 19940309 <-- |
| PRIORITY APPLN. INFO.: | | | CA 1989-605091 | 19890707 <-- |
| | | | CA 1990-2019005 | 19900614 <-- |
| | | | US 1990-547670 | 19900703 <-- |
| | | | US 1992-927694 | 19920807 <-- |
| OTHER SOURCE(S): | | MARPAT 115:72235 | | |
| GI | | | | |

$$\text{XNR}^1\text{CHR}^2\text{CW}^1\text{NHC}^3\text{R}^4\text{CW}^2\text{NR}^5\text{CH}(\text{CH}_2\text{COY})\text{CW}^3\text{NHC}^6$$

$$[\text{CR}^7(\text{R}^8)\text{CO}_2\text{H}]\text{CW}^4\text{NHC}^9\text{R}^{10}\text{Z}$$

I

AB Substituted aspartic acid-contg. pentapeptides I [X = C1-10 alkanoyl, C1-10 alkoxy carbonyl, (substituted) COCH₂Ph, etc.; R1 = H, C1-6 alkyl, phenyl-C1-6 alkyl; R2 = (hydroxy or mercapto) C1-6 alkyl; R3, R5, R6, R9 H, C1-6 alkyl; R4 = H, (OH, SH, OMe, SMe) C1-6 alkyl, C3-6 cycloalkyl, C3-6 cycloalkylmethyl; R7, R8 = H, C1-6 alkyl or CR⁷R⁸ = C3-6 cycloalkyl; R10 = C1-6 alkenyl, etc.; W1-W4 = O, S; Y = C1-14 alkoxy, C3-14 alkoxy, C3-14 alkenyloxy, Me(OCH₂CH₂)nO, (substituted) phenoxy, substituted amino, etc.; n = 1-3; Z = H, CO₂H, CH₂CO₂H, CH₂OH, CO₂R¹¹, etc.; R¹¹ = C1-6 alkyl] were prepd. Thus, title pentapeptide I [X = 4-OHC₆H₄(CH₂)₂CO, R1 = Me, R2 = Me₂CH, R3, R5-R9 = H, R4 = CHMeEt, R10 = CH₂CHMe₂, W1-W4 = O, Y = NEt₂, Z = CO₂H] (II) was prepd. via solid phase methods using a BHA photoresin and BOP/HOBt as the coupling agent. The resin was cleaved via photolysis and deprotection of the cleaved peptide was accomplished by hydrogenation over Pd/C. The IC₅₀ of II against HSV-1 2as 0.27 .mu.M. IC 50's of 41 other I were detd.

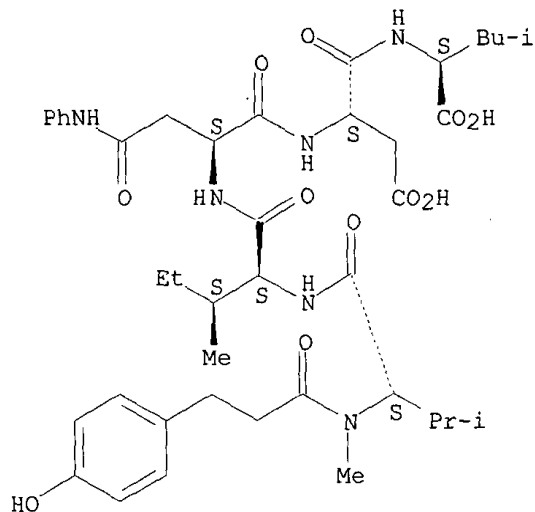
IT 134996-97-7P 134997-05-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiherpes agent)

RN 134996-97-7 HCAPLUS

CN L-Leucine, N-[N-[N2-[N-[N-[3-(4-hydroxyphenyl)-1-oxopropyl]-N-methyl-L-valyl]-L-isoleucyl]-N-phenyl-L-asparaginyl]-L-.alpha.-aspartyl]- (9CI)
(CA INDEX NAME)

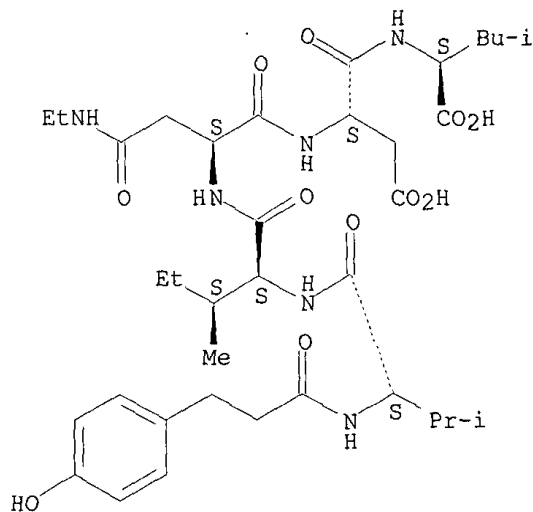
Absolute stereochemistry.



RN 134997-05-0 HCAPLUS

CN L-Leucine, N-[N-[N-ethyl-N2-[N-[N-[3-(4-hydroxyphenyl)-1-oxopropyl]-L-valyl]-L-isoleucyl]-L-asparaginy]-L-.alpha.-aspartyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



9, 11

L31 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:7265 HCAPLUS

DOCUMENT NUMBER: 114:7265

TITLE: Preparation of tumor necrosis factor analogs

INVENTOR(S): Boehm, Hans Joachim; Daum, Lothar; Haupt, Andreas;
Schmied, Bernhard; Walker, Nigel; Zechel, Johann
Christian

PATENT ASSIGNEE(S): BASF A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 17 pp.

DOCUMENT TYPE: **Patent**
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-----------------|-----------------|--------------|
| DE 3841755 | A1 | 19900613 | DE 1988-3841755 | 19881212 |
| WO 9006938 | A1 | 19900628 | WO 1989-EP1471 | 19891202 <-- |
| W: JP, US | | | | |
| RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE | | | | |
| EP 447431 | A1 | 19910925 | EP 1990-900108 | 19891202 <-- |
| R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| JP 04502307 | T2 | 19920423 | JP 1990-500555 | 19891202 <-- |
| CA 2005056 | AA | 19900612 | CA 1989-2005056 | 19891211 <-- |
| PRIORITY APPLN. INFO.: | | | DE 1988-3841755 | 19881212 <-- |
| | | | WO 1989-EP1471 | 19891202 <-- |
| OTHER SOURCE(S): | | MARPAT 114:7265 | | |
| GI | | | | |

Ac-Pro-Dap-Ala-His-Aoc-Gly-Asp-Ile-Ala-Leu-NH₂ I

AB X-Ala-His-A-Y [A = Val, Leu, Ile, NH(CH₂)_mCO; m = 1-12; X = GNHCHMCO, GNHCHMCO₂, GRNHCHMCO, GRNHCHMCO₂; Y = Z, NHCHQCOZ, VNHCHQCOZ, NHCHQCOU₂, VNHCHQCOU₂; G = H, protecting group; Z = OH, NH₂, protecting group; R = Leu-Arg-Ser-Ser-Ser-Gln-Asn-Ser-Ser-Asp-Lys-Pro, Val-Arg-Ser-Ser-Ser-Arg-Thr-Pro-Ser-Asp-Lys-Pro, Leu-Arg-Ser-Ser-Ser-Gln-Ala-Ser-Ser-Asn-Lys-Pro, Leu-Arg-Ser-Ala-Ser-Arg-Ala-Leu-Ser-Asp-Lys-Pro, 5-11 amino acid residue segments of the above, 1-4 amino acid residues; U, V, W = 1-4 amino acid residues; M, Q = H, CHMe₂, CHMeEt, Ph, CH(OH)Me, 3-indolylmethyl, 4-imidazolylmethyl, etc.], were prepd. as tumor necrosis factor agonists/antagonists (no data). Thus, cyclic title peptide I (Dap = 2,3-diaminopropionyl, Aoc = 8-aminooctanoyl) was prepd. using BOC-protected amino acids and methylbenzhydrylamine resin followed by cyclization using (PhO)₂P(O)N₃.

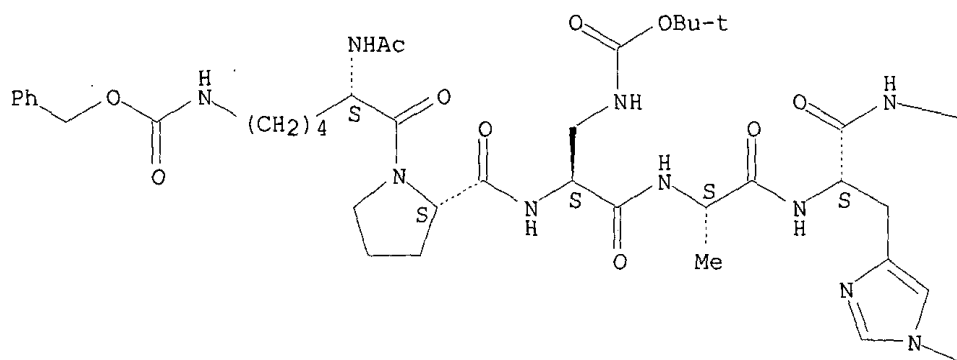
IT **130851-27-3DP**, resin bound
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and resin cleavage reaction of, in tumor necrosis factor analog)

RN 130851-27-3 HCAPLUS

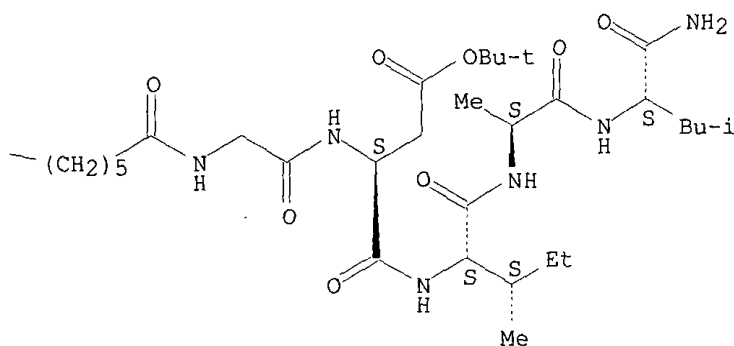
CN L-Leucinamide, N-[6-[[N-[N-[N-[1-[N²-acetyl-N⁶-[(phenylmethoxy)carbonyl]-L-lysyl]-L-prolyl]-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-L-alanyl]-L-alanyl]-1-(triphenylmethyl)-L-histidyl]amino]-1-oxohexyl]glycyl-L-α-aspartyl-L-isoleucyl-L-alanyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CPh3

L31 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:7257 HCAPLUS

DOCUMENT NUMBER: 114:7257

TITLE: Preparation of cytotoxic LHRH analogs

INVENTOR(S): Schally, Andrew V.; Bajuz, Sandor; Janaky, Tamas

PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA

SOURCE: Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|--------------|
| EP 364819 | A2 | 19900425 | EP 1989-118460 | 19891005 <-- |
| EP 364819 | A3 | 19910306 | | |

R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
 JP 02157293 A2 19900618 JP 1989-273650 19891020 <--
 US 5258492 A 19931102 US 1991-710515 19910603 <--
 NO 9304541 A 19940207 NO 1993-4541 19931210 <--
 PRIORITY APPLN. INFO.: US 1988-260994 A 19881021 <--
 US 1989-404667 A 19890907 <--
 WO 1991-US4264 A 19910614 <--

OTHER SOURCE(S): MARPAT 114:7257

AB R-X1-X2-X3-Ser-X5-X6-Q-Leu-Arg-Pro-X10-NH2 [I; R = H, alkanoyl, carbamyl; X1 = pyroglutamyl, Pro, D-3-(2-naphthyl)alanyl, D-4-chlorophenylalanyl; X2 = His, D-4-chlorophenylalanyl; X3 = Trp, D-Trp, D-3-(3-pyridyl)alanyl; X5 = Tyr, Arg; X6 = D-Phe, D-Lys, D-Orn, D-Phe(NH2); X10 = Gly, D-Ala; Q = bis-(2-chloroethyl)amino when X6 = D-Phe, or complexed metal contg. acyl, e.g., CH2(NH2)(CH2)m CH(NH2)(CH2)nCO[NH(CH2)oCO]p; m = 0, 1; n, p = 0-10; o = 1-10; metal = Pt, Ga, Ge, Sr, Ti, Va, Fe, Cu, Co, Au, Ni, Cd, Zn], were prepd. Thus, pGlu-His-Trp-Ser-Tyr-OH (pGlu = pyroglutamyl) and H-D-Mel-Leu-Arg-Pro-Gly-NH2.HCl [Mel = 4-[bis(2-chloroethyl)amino]-D-phenylalanyl] were coupled in DMF using (Me2CH)2NEt, DCC, and hydroxybenzotriazole at 0.degree. for 24 h to give [D-Mel6]LHRH. I at 1.5-10 .mu.g/rat showed 20-100% inhibition of ovulation.

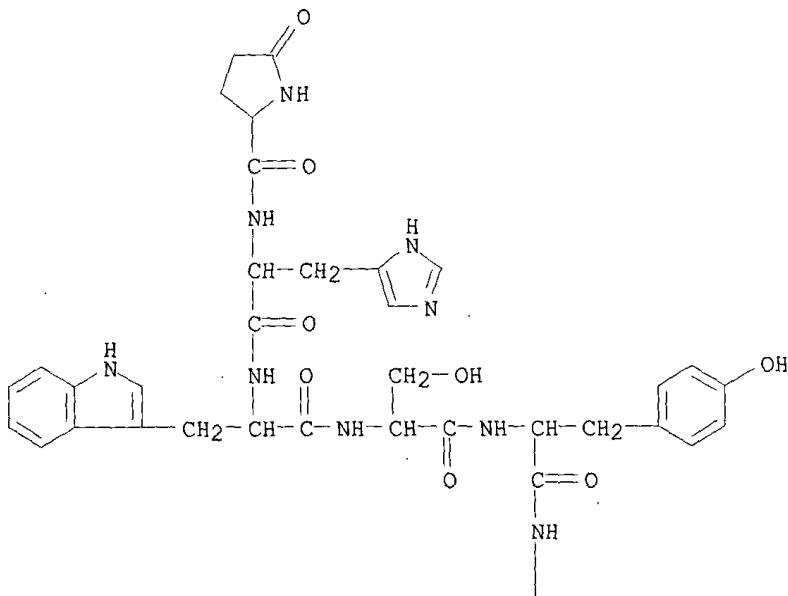
IT 130751-50-7P

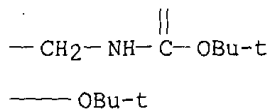
RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as intermediate for cytotoxic LHRH analog)

RN 130751-50-7 HCAPLUS

CN Luteinizing hormone-releasing factor (swine), 6-[N6-[N-[(1,1-dimethylethoxy)carbonyl]-3-[(1,1-dimethylethoxy)carbonyl]amino]alanyl]-D-lysine]- (9CI) (CA INDEX NAME)

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L31 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:94948 HCAPLUS

DOCUMENT NUMBER: 108:94948

TITLE: Preparation of vasopressin fragment derivatives as
nootropics for treatment of senility

INVENTOR(S): Goto, Giichi; Nagaoka, Akinobu; Wakimasu, Mitsuhiro

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 68 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 227410 | A2 | 19870701 | EP 1986-309800 | 19861216 <-- |
| EP 227410 | A3 | 19890208 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 4748154 | A | 19880531 | US 1986-939103 | 19861208 <-- |
| CA 1292841 | A1 | 19911203 | CA 1986-525277 | 19861215 <-- |
| JP 62234095 | A2 | 19871014 | JP 1986-302660 | 19861218 <-- |
| JP 08030079 | B4 | 19960327 | | |

PRIORITY APPLN. INFO.: JP 1985-291474 19851224 <--

OTHER SOURCE(S): CASREACT 108:94948

AB PGlu-Asp(NHR1)-Cys(H-Cys-OH)-A-D-Lys-B [I; R1 = H, C1-18 alkyl, (substituted) phenyl-C1-3 alkyl; A = amino, C1-6 alkylaminoacid residue; B = OH, amino, amino acid or amide] were prepd. as vasopressin fragment peptides, useful for treatment and prevention of dementia. PGlu-Asn-Cys(H-Cys-OH)-Pro-D-Lys-OH (II) was prepd. using soln.-phase methods, starting from BOC-D-Lys(Z)-OH.DCHA (BOC = tert-butyloxycarbonyl, Z = benzyloxycarbonyl, DCHA = dicyclohexylamine). II reversed cycloheximide-induced amnesia in mice when given intracerebroventricularly at 10 pg-10 ng.

IT 112954-73-1P 112972-69-7P

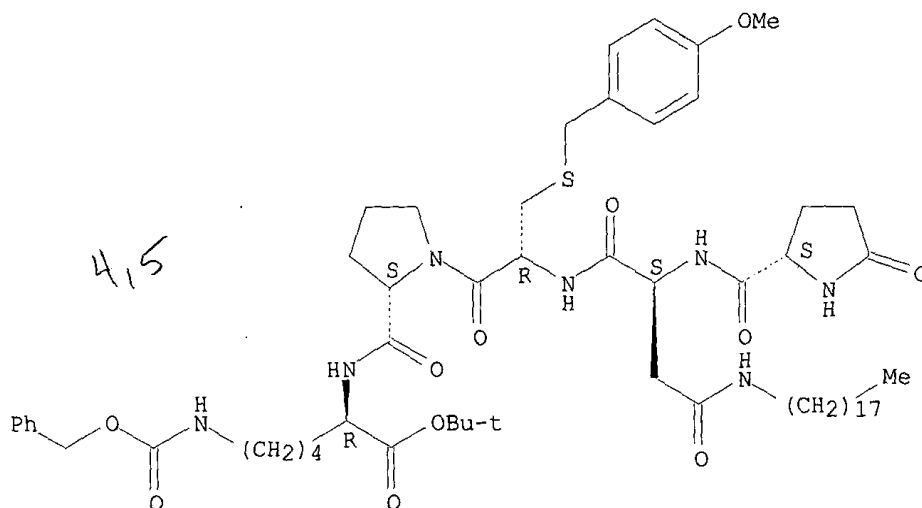
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as intermediate for antisenility agent)

RN 112954-73-1. HCAPLUS

CN D-Lysine, N2-[1-[S-[(4-methoxyphenyl)methyl]-N-[N-octadecyl-N2-(5-oxo-L-prolyl)-L-asparaginyl]-L-cysteinyl]-L-prolyl]-N6-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

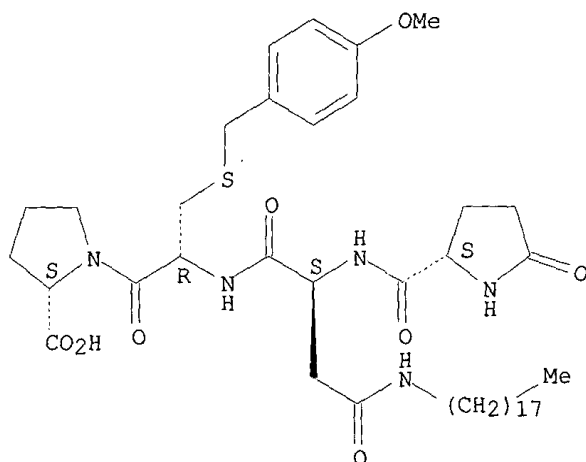
Absolute stereochemistry.



RN 112972-69-7 HCAPLUS

CN L-Proline, 1-[S-[(4-methoxyphenyl)methyl]-N-[N-octadecyl-N2-(5-oxo-L-prolyl)-L-asparaginyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

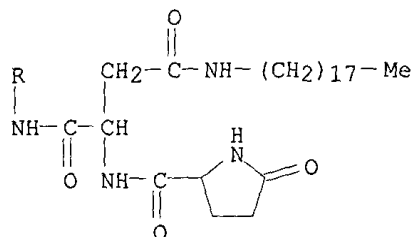
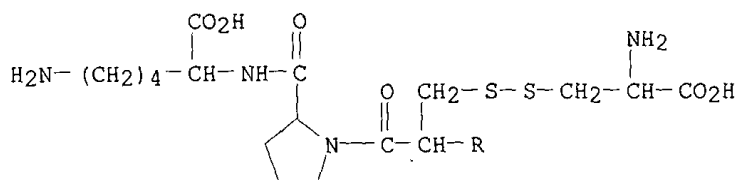


IT 112954-35-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as nootropic, for treatment of senility)

RN 112954-35-5 HCAPLUS

CN D-Lysine, 5-oxo-L-prolyl-N-octadecyl-L-asparaginyl-L-cysteinyl-L-prolyl-,
disulfide with L-cysteine (9CI) (CA INDEX NAME)



L31 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:627342 HCAPLUS

DOCUMENT NUMBER: 105:227342

TITLE: Pepstatin analogs

INVENTOR(S): Wagnon, Jean le Hameau de la Rauze; Callet, Georges;
Gagnol, Jean Pierre; Nisato, Dino; Cazaubon, Catherine
PATENT ASSIGNEE(S): SANOFI, Fr.; Institut National de la Sante et de la
Recherche Medicale (INSERM)

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 192554 | A1 | 19860827 | EP 1986-400271 | 19860210 <-- |
| EP 192554 | B1 | 19920102 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| FR 2577225 | A1 | 19860814 | FR 1985-1981 | 19850212 |
| FR 2577225 | B1 | 19870828 | | |
| FR 2577226 | A1 | 19860814 | FR 1985-1982 | 19850212 |
| FR 2577226 | B1 | 19900615 | | |
| CA 1286846 | A1 | 19910723 | CA 1986-500927 | 19860203 <-- |
| US 4725580 | A | 19880216 | US 1986-826349 | 19860205 <-- |
| US 4746648 | A | 19880524 | US 1986-826375 | 19860205 <-- |
| CA 1286847 | A1 | 19910723 | CA 1986-501163 | 19860205 <-- |
| AU 8653272 | A1 | 19860814 | AU 1986-53272 | 19860206 <-- |
| AU 606312 | B2 | 19910207 | | |
| AU 8653273 | A1 | 19860821 | AU 1986-53273 | 19860206 <-- |
| AU 606572 | B2 | 19910214 | | |
| DK 8600640 | A | 19860813 | DK 1986-640 | 19860210 <-- |
| DK 8600641 | A | 19860813 | DK 1986-641 | 19860210 <-- |
| EP 193445 | A1 | 19860903 | EP 1986-400272 | 19860210 <-- |
| EP 193445 | B1 | 19900509 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |

| | | | | | |
|------------------------|----|----------|---------------------|----------|-----|
| ZA 8600960 | A | 19861029 | ZA 1986-960 | 19860210 | <-- |
| ZA 8600961 | A | 19861029 | ZA 1986-961 | 19860210 | <-- |
| AT 52518 | E | 19900515 | AT 1986-400272 | 19860210 | <-- |
| AT 71111 | E | 19920115 | AT 1986-400271 | 19860210 | <-- |
| ES 551820 | A1 | 19861216 | ES 1986-551820 | 19860211 | <-- |
| ES 551821 | A1 | 19870101 | ES 1986-551821 | 19860211 | <-- |
| JP 61186397 | A2 | 19860820 | JP 1986-28747 | 19860212 | <-- |
| JP 61186398 | A2 | 19860820 | JP 1986-28748 | 19860212 | <-- |
| PRIORITY APPLN. INFO.: | | | FR 1985-1981 | 19850212 | <-- |
| | | | FR 1985-1982 | 19850212 | <-- |
| | | | EP 1986-400271 | 19860210 | <-- |
| | | | EP 1986-400272 | 19860210 | <-- |
| OTHER SOURCE(S): | | | CASREACT 105:227342 | | |
| GT | | | | | |

$$R^1-NHCHR^2CO-NHCHR^3CO-NHCH(CH_2R^4)CH(OH)CH_2CO-X^1-X^2-R^5 \quad I$$

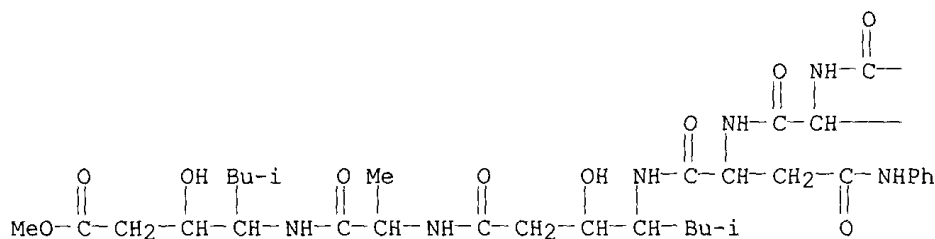
AB Title peptides 1 (R1 = alkanoyl, arylcarbonyl, carbalkoxy, etc.; R2 = alkyl, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R3 = H, alkenyl, Ph, naphthyl, etc.; R4 = CHMe2, Ph, cyclohexyl; R5 = OH, alkoxy, NH2, etc.; X1X2 = Ala-Sta, Ala-Leu, Leu-Phe, Val-Sta, etc.) (Sta = statine) were prepd., and they exhibited renin-inhibiting activity. Thus, BOC-Phe-Asp(CH2Ph)-Sta-Ala-Leu-OMe was prepd. by soln. method peptide synthesis.

IT **105382-26-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)

RN 105382-26-1 HCAPLUS

CN L-Aspartamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N1-[2-hydroxy-4-[[2-[[2-hydroxy-4-methoxy-1-(2-methylpropyl)-4-oxobutyl]amino]-1-methyl-2-oxoethyl]amino]-1-(2-methylpropyl)-4-oxobutyl]-N4-phenyl-, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

----- OBU-t

$$-\text{CH}_2-\text{Ph}$$

L31 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1982:406791 HCAPLUS
 DOCUMENT NUMBER: 97:6791
 TITLE: Peptides and their therapeutic use
 INVENTOR(S): Roques, Bernard; Lecomte, Jeanne Marie
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.
 SOURCE: Eur. Pat. Appl., 23 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: **Patent**
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 46113 | A1 | 19820217 | EP 1981-401263 | 19810805 <-- |
| EP 46113 | B1 | 19841219 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| FR 2488253 | A1 | 19820212 | FR 1980-17523 | 19800808 |
| FR 2488253 | B1 | 19840127 | | |
| US 4407794 | A | 19831004 | US 1981-289383 | 19810803 <-- |
| AT 10836 | E | 19850115 | AT 1981-401263 | 19810805 <-- |
| CA 1292344 | A1 | 19911119 | CA 1981-383284 | 19810806 <-- |
| JP 57059845 | A2 | 19820410 | JP 1981-123927 | 19810807 <-- |
| PRIORITY APPLN. INFO.: | | | FR 1980-17523 | 19800808 <-- |
| | | | EP 1981-401263 | 19810805 <-- |

OTHER SOURCE(S): CASREACT 97:6791

AB Enkephalin-related peptides H-Tyr-X-Gly-L-NHCH(CH₂R)CO-X₁-R₁ [X = D-Ala, D-Ser, D-Thr, D-Cys, NHCMe₂CO, AzaGly, OH-substituted amino acid residues; R = Ph, C₆H₄F-p, C₆F₅; X₁ = Leu or Ile with D- or L-configuration; R₁ = H, NHCHR₂(CH₂)_nCH₂OR₃ or NHCHR₂CH(OR₃)Me (R₂ = H, OH, CO₂H, CONH₂, phosphatidylethanolamine moiety; R₃ = H, OH-protective group; n = 0, 1, 2)] were prepd. as analgesics. Thus, Boc-Gly-Phe-Leu-OMe (Boc = Me₃CO₂C) was Boc-deblocked by CF₃CO₂H and then coupled with Boc-Tyr-D-Ser(CMe₃)-OH by DCC-hydroxybenzotriazole to give Boc-Tyr-D-Ser(CMe₃)-Gly-Phe-Leu-OR₄ (I, R₄ = Me), which was sapon. to give I (R₄ = H). The latter was coupled with H-Thr(CMe₃)-OMe to give Boc-Tyr-D-Ser(CMe₃)-Gly-Phe-Leu-Thr(CMe₃)-OMe, which was sapon. and then deblocked by CF₃CO₂H/HCl to give H-Tyr-D-Ser-Gly-Phe-Leu-Thr-OH (II). II at 25 mg/kg (i.v.) exhibited in vivo analgesic activity in mice.

IT 82015-15-4P 82015-16-5P 82015-17-6P

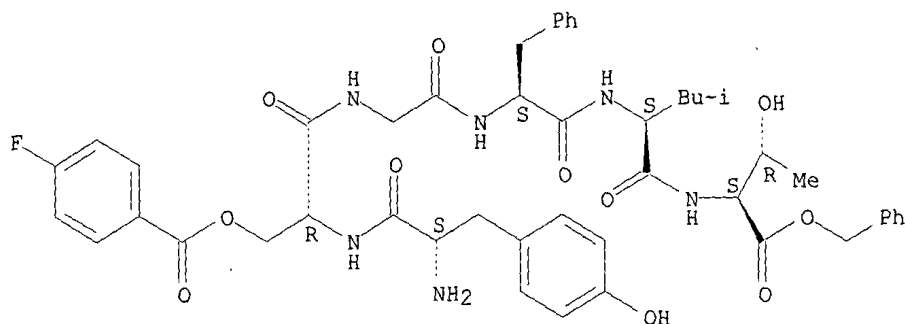
82015-23-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

RN 82015-15-4 HCAPLUS

CN L-Threonine, N-[N-[N-[N-[O-(4-fluorobenzoyl)-N-L-tyrosyl-D-seryl]glycyl]-L-phenylalanyl]-L-leucyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

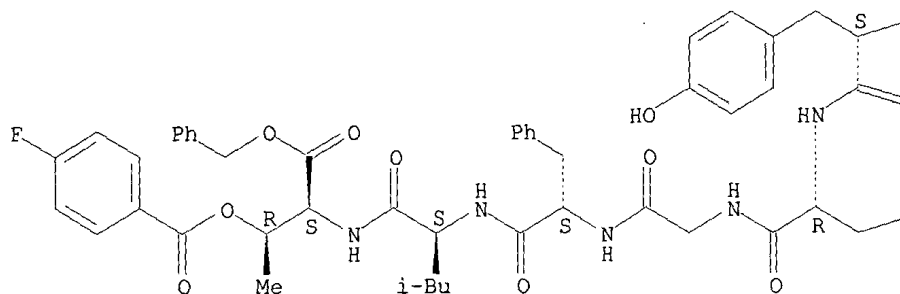


RN 82015-16-5 HCAPLUS

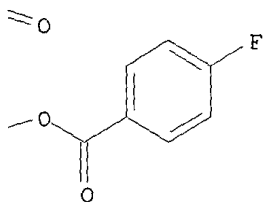
CN L-Threonine, N-[N-[N-[N-[O-(4-fluorobenzoyl)-N-L-tyrosyl-D-seryl]glycyl]-L-phenylalanyl]-L-leucyl]-, phenylmethyl ester, 4-fluorobenzoate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



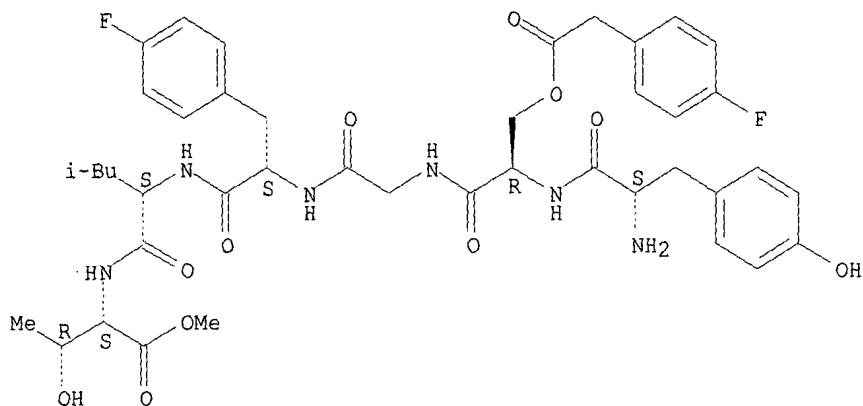
PAGE 1-B

-NH₂

RN 82015-17-6 HCAPLUS

CN L-Threonine, N-[N-[4-fluoro-N-[N-[O-[(4-fluorophenyl)acetyl]-N-L-tyrosyl-D-seryl]glycyl]-L-phenylalanyl]-L-leucyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

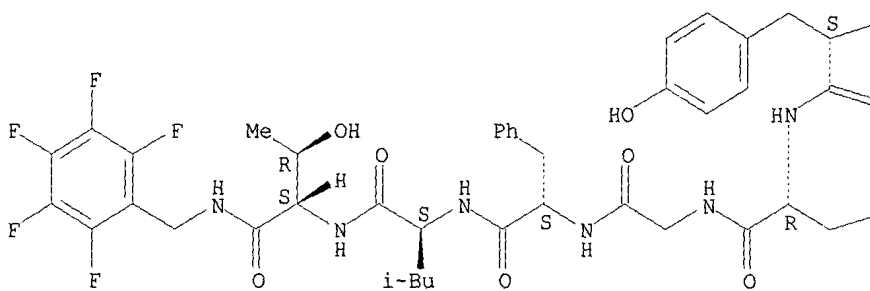


RN 82015-23-4 HCAPLUS

CN L-Threoninamide, L-tyrosyl-O-(4-fluorobenzoyl)-D-serylglycyl-L-phenylalanyl-L-leucyl-N-[(pentafluorophenyl)methyl]- (9CI) (CA INDEX NAME)

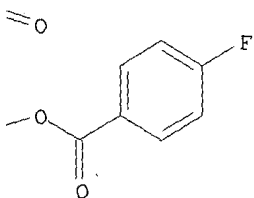
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

NH₂



L31 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1981:587675 HCAPLUS

DOCUMENT NUMBER: 95:187675

TITLE: LH-RH antagonists

INVENTOR(S): Coy, David Howard; Schally, Andrew Victor

PATENT ASSIGNEE(S): USA

SOURCE: Brit. UK Pat. Appl., 14 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| GB 2053229 | A | 19810204 | GB 1980-19009 | 19800610 <-- |
| GB 2053229 | B2 | 19830302 | | |
| US 4317815 | A | 19820302 | US 1980-155249 | 19800602 <-- |
| AT 8988 | E | 19840915 | AT 1981-200526 | 19810518 <-- |
| PRIORITY APPLN. INFO.: | | | CA 1979-329643 | 19790613 <-- |
| | | | US 1980-155249 | 19800602 <-- |
| | | | EP 1981-200526 | 19810518 <-- |

AB LH-releasing hormone antagonists R-X-X1-X2-Ser-Tyr-X3-Leu-Arg-Pro-X4-NH2 [R = H, alkanoyl, HO2C(CH2)nCO2 (n = 2-6), Bz, H-Gly, D- or L-amino acyl; X = D-Trp, optionally p-substituted D-Phe; X1 = optionally p-substituted D-Phe; X2 = D-Trp, Trp, Phe; X3 = D-Trp, optionally p-substituted D-Phe; X4 = Gly, D-Ala] were prepd. Thus, Ac-D-Phe-D-Phe(Cl-p)-D-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH2 (I) was prepd. by the solid-phase method on a benzhydrylamine resin. I at 0.062 mg produced complete inhibition of ovulation in mature female rats.

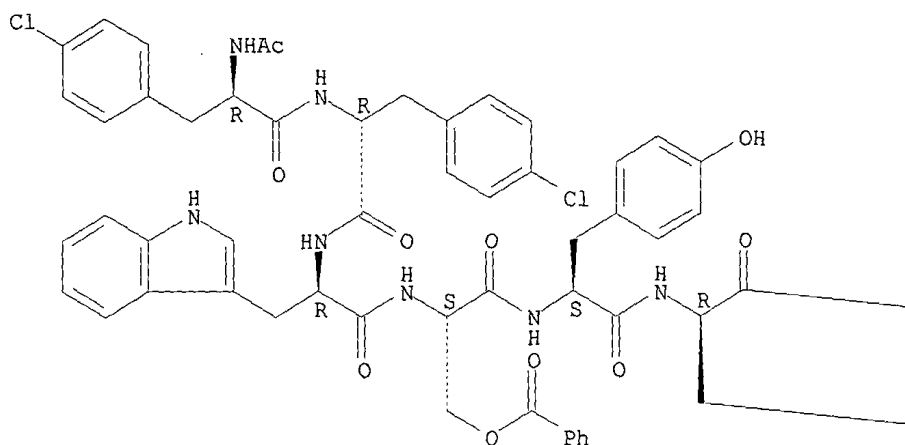
IT **79561-85-6DP**, benzhydrylamine resin-bound **79561-86-7DP**, benzhydrylamine resin-bound **79561-87-8DP**, benzhydrylamine resin-bound
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and resin cleavage and deblocking of)

RN 79561-85-6 HCAPLUS

CN Glycinamide, N-acetyl-4-chloro-D-phenylalanyl-4-chloro-D-phenylalanyl-D-tryptophyl-O-benzoyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-N5-[[imino[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-prolyl- (9CI) (CA INDEX NAME)

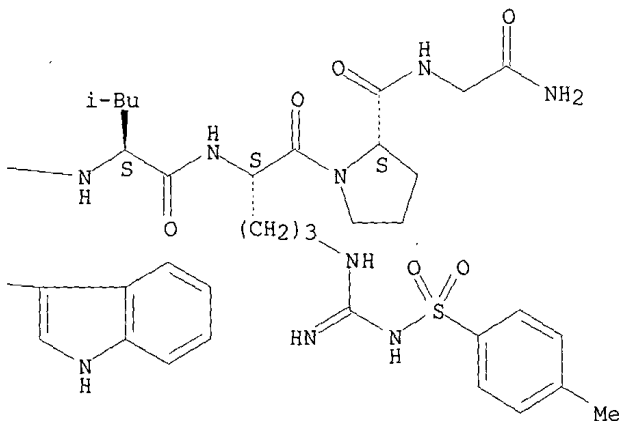
Absolute stereochemistry.

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2,3

PAGE 1-B

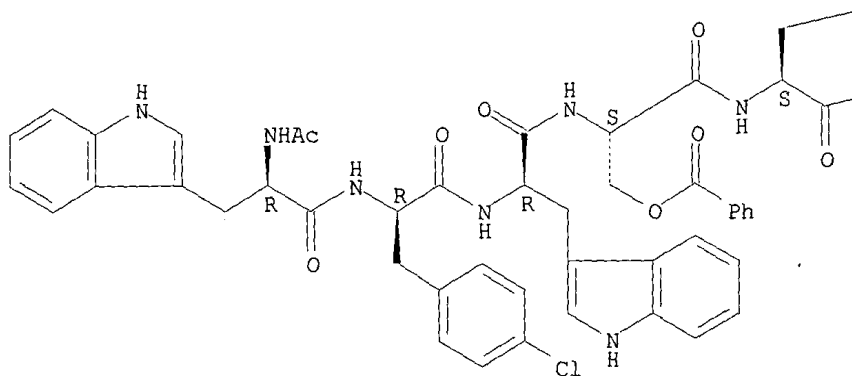


RN 79561-86-7 HCAPLUS

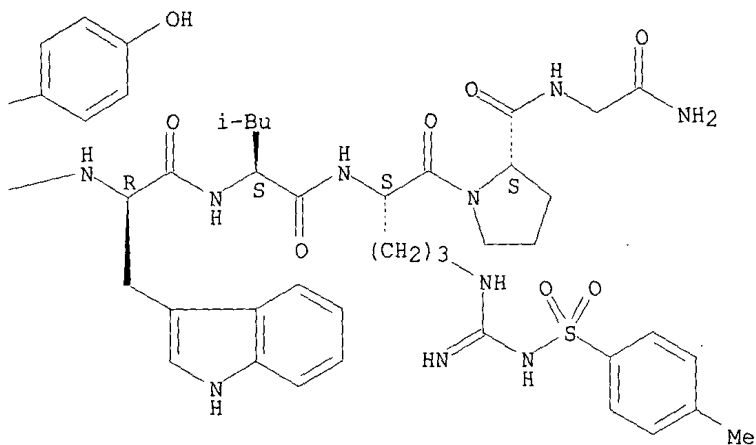
CN Glycinamide, N-acetyl-D-tryptophyl-4-chloro-D-phenylalanyl-D-tryptophyl-O-benzoyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-N5-[imino[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



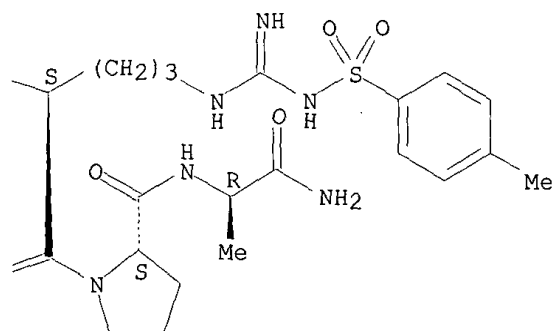
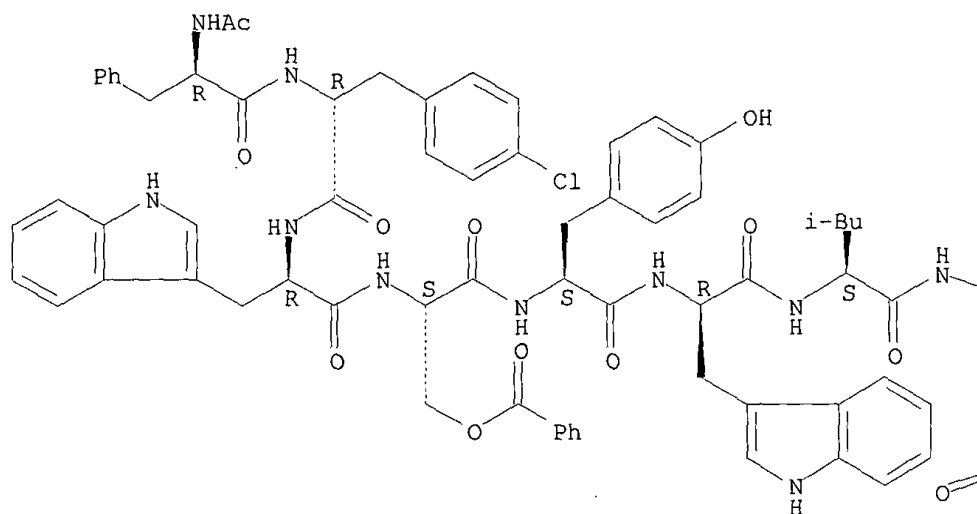
PAGE 1-B



RN 79561-87-8 HCAPLUS

CN D-Alaninamide, N-acetyl-D-phenylalanyl-4-chloro-D-phenylalanyl-D-tryptophyl-O-benzoyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-N5-[imino[[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:509987 HCAPLUS
DOCUMENT NUMBER: 95:109987
TITLE: Nouel substrates for endotoxin detection
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|--------------|
| JP 56042597 | A2 | 19810420 | JP 1979-117335 | 19790914 |
| JP 63026871 | B4 | 19880531 | | |
| JP 02000192 | A2 | 19900105 | JP 1989-57818 | 19890313 <-- |
| JP 03011760 | B4 | 19910218 | | |

PRIORITY APPLN. INFO.: JP 1979-117335 19790914 <--

AB A sample contg. bacterial endotoxins is treated with the novel substrate R1-Gly-Arg-NHPhNet2 (R1 = L-amino acid residue or peptide group contg. L-amino acid residues) and amebocyte lysates from horseshoe crab to form p-(N,N-diethylamino)aniline, which is coupled with 1-naphthol-2-sulfonic acid to give a product for spectrometric detn. For example, Tachypleus tridentatus amebocyte lysate was reacted with endotoxin prepd. from Salmonella minnesota by the method of M. Niwa et al. (1973), followed by treatment with BOC-Leu-Gly-Arg-DEAA [78545-16-1] (BOC = tert-butoxycarbonyl; DEAA = NHPhNet2) to give p-(N,N-diethylamino)aniline, which was treated with Na 1-naphthol-2-sulfonate [832-50-8] to give a product for spectrometric detn. at 675 nm for the measurement of endotoxin. The substrate was prepd. by the reaction of BOC-Leu-Gly-OH [32991-17-6] with H-Arg(NO2)-DEAA [2188-18-3] in the presence of carbodiimide to form BOC-Leu-Gly-Arg(NO2)-DEAA [78545-17-2], which is reduced with Pd catalyst to produce BOC-Leu-Gly-Arg-DEAA.

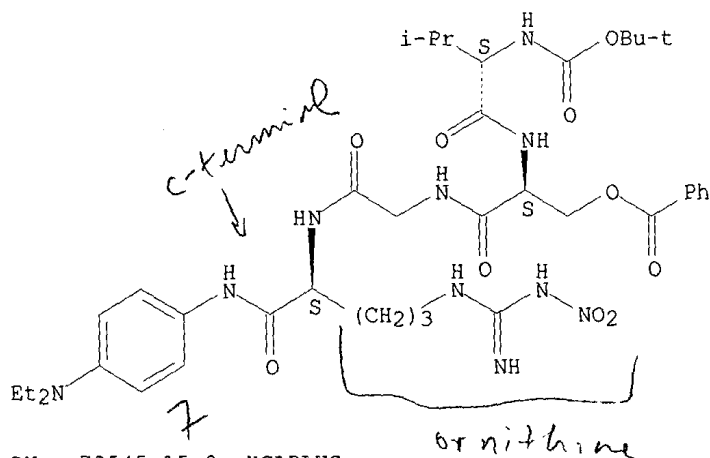
IT 78545-13-8 78545-15-0

RL: RCT (Reactant)
 (redn. of)

RN 78545-13-8 HCAPLUS

CN L-Ornithinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-O-benzoyl-L-serylglycyl-N-[4-(diethylamino)phenyl]-N5-[imino(nitroamino)methyl]- (9CI)
 (CA INDEX NAME)

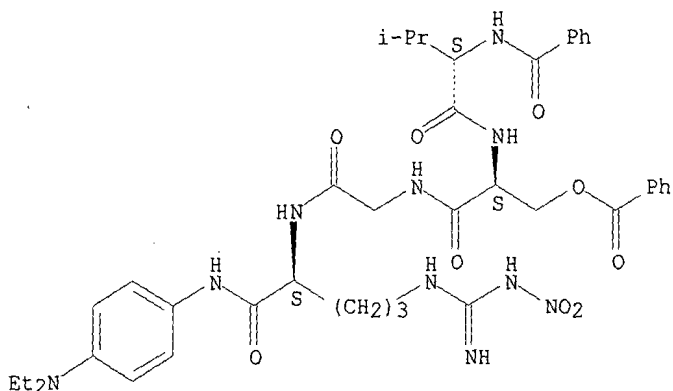
Absolute stereochemistry.



RN 78545-15-0 HCAPLUS

CN L-Ornithinamide, N-benzoyl-L-valyl-O-benzoyl-L-serylglycyl-N-[4-(diethylamino)phenyl]-N5-[imino(nitroamino)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1979:558110 HCAPLUS
 DOCUMENT NUMBER: 91:158110
 TITLE: Blocking allergic responses
 INVENTOR(S): Hamburger, Robert N.
 PATENT ASSIGNEE(S): University of California, Berkeley, USA
 SOURCE: U.S., 12 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: **Patent**
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|--------------|
| US 4161522 | A | 19790717 | US 1978-940323 | 19780907 <-- |
| US 4171299 | A | 19791016 | US 1976-652868 | 19760127 <-- |
| AU 8065181 | A1 | 19810416 | AU 1980-65181 | 19801208 <-- |
| AU 531075 | B2 | 19830811 | | |

PRIORITY APPLN. INFO.:
 US 1975-565425 19750404 <--
 US 1976-652868 19760127 <--
 AU 1976-12303 19760324 <--

AB Tripeptides to decapeptides from the 265-537 sequence of the Fc region of Ig E, useful as agents for blocking the mammalian allergic response, were prepd. by solid-phase methods. Thus, BOC-Asp-(OCH₂Ph)-Pro-Arg(NO₂)-O-resin (I, BOC = Me₃CO₂C) was prepd. by stepwise solid-phase couplings and then was resin-cleaved and deblocked by HBr/CF₃CO₂H to give H-Asp-Pro-Arg(NO₂)-OH, which was hydrogenated to give H-Asp-Pro-Arg-OH. I was used in the solid-phase prepn. of BOC-Ser(CH₂Ph)-Asp(OCH₂Ph)-Pro-Arg(NO₂)-O-resin (II), which was cleaved and deblocked to give H-Ser-Asp-Pro-Arg-OH, and II was used in the solid-phase prepn. of H-Asp-Ser-Asp-Pro-OH (III). H-Ala-Asp-Ser-Asp-Pro-Arg-OH was also prepd. III exhibited an av. allergic inhibition of 72% in an assay of the Prausnitz-Kustner reaction.

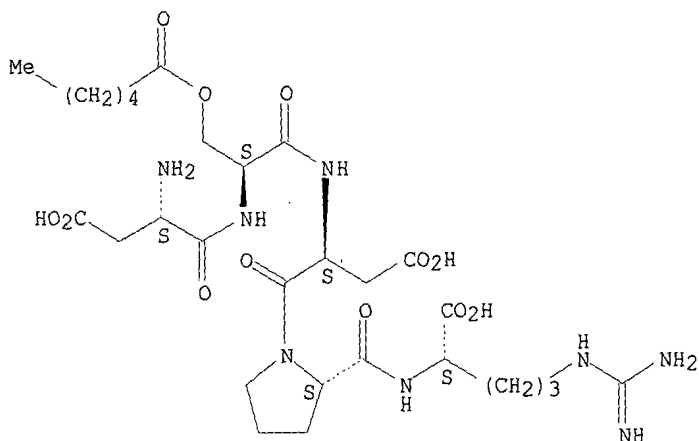
IT **62087-79-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

RN 62087-79-0 HCAPLUS

CN L-Arginine, N2-[1-[N-[N-L-.alpha.-aspartyl-O-(1-oxohexyl)-L-seryl]-L-.alpha.-aspartyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1979:134551 HCAPLUS

DOCUMENT NUMBER: 90:134551

TITLE: Tetrapeptides and their preparation and use in determining serine proteases

INVENTOR(S): Claeson, Karl Goran; Aurell, Leif Erik; Simonsson, Leif Roger

PATENT ASSIGNEE(S): Aktiebolag Kabi, Swed.

SOURCE: Ger. Offen., 20 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|--------------|
| DE 2753653 | A1 | 19780608 | DE 1977-2753653 | 19771201 <-- |
| DE 2753653 | C2 | 19830721 | | |
| SE 7613463 | A | 19780602 | SE 1976-13463 | 19761201 |
| SE 437153 | B | 19850211 | | |
| SE 437153 | C | 19850530 | | |
| IL 53187 | A1 | 19810227 | IL 1977-53187 | 19771021 <-- |
| NL 7711791 | A | 19780605 | NL 1977-11791 | 19771027 <-- |
| NL 178600 | B | 19851118 | | |
| NL 178600 | C | 19860416 | | |
| FI 7703242 | A | 19780602 | FI 1977-3242 | 19771031 <-- |
| ZA 7706460 | A | 19780830 | ZA 1977-6460 | 19771031 <-- |
| ES 464117 | A1 | 19780901 | ES 1977-464117 | 19771114 <-- |
| US 4207232 | A | 19800610 | US 1977-852006 | 19771116 <-- |
| AU 7730771 | A1 | 19790524 | AU 1977-30771 | 19771118 <-- |
| AU 514768 | B2 | 19810226 | | |
| GB 1565154 | A | 19800416 | GB 1977-48288 | 19771121 <-- |
| BE 861295 | A1 | 19780316 | BE 1977-183005 | 19771129 <-- |
| FR 2372798 | A1 | 19780630 | FR 1977-35870 | 19771129 <-- |
| FR 2372798 | B1 | 19831110 | | |
| DD 136896 | C | 19790801 | DD 1977-202299 | 19771129 <-- |

| | | | | |
|------------------------|----|----------|-----------------|--------------|
| PL 109588 | B1 | 19800630 | PL 1977-202501 | 19771129 <-- |
| CH 637627 | A | 19830815 | CH 1977-14618 | 19771129 <-- |
| NO 7704092 | A | 19780602 | NO 1977-4092 | 19771130 <-- |
| SU 736889 | D | 19800525 | SU 1977-2548501 | 19771130 <-- |
| CA 1098428 | A1 | 19810331 | CA 1977-292077 | 19771130 <-- |
| DK 7705353 | A | 19780602 | DK 1977-5353 | 19771201 <-- |
| DK 155333 | B | 19890328 | | |
| DK 155333 | C | 19890904 | | |
| JP 53069693 | A2 | 19780621 | JP 1977-143340 | 19771201 <-- |
| JP 57008720 | B4 | 19820217 | | |
| AT 7708596 | A | 19800115 | AT 1977-8596 | 19771201 <-- |
| AT 358203 | B | 19800825 | | |
| HU 19255 | O | 19801227 | HU 1977-KA1497 | 19771201 <-- |
| HU 176983 | P | 19810628 | | |
| DE 2760116 | C2 | 19850912 | DE 1977-2760116 | 19771201 <-- |
| US 4276375 | A | 19810630 | US 1979-86970 | 19791022 <-- |
| PRIORITY APPLN. INFO.: | | | SE 1976-13463 | 19761201 <-- |
| | | | US 1977-852006 | 19771116 <-- |

AB The carboxyl side chains of tetrapeptides representing the protease cleavage site of prothrombin are esterified or amidated to give substrates for detn. of blood-coagulation factor Xa. Thus, 30 .mu.L SOCl₂ was mixed with 0.5 mL MeOH, and 75 mg (0.10 mmol) Bz-Ile-Glu-Gly-Arg-R (R = p-nitroaniline) was added. After 5 h, methylated peptide was purified by chromatog. (30% yield). The product was incubated in a com. protease detn. system, and liberation of p-nitroaniline was measured at 405 nm. The modified peptide was 2.3-fold more active than the unmodified peptide, which is presently used in clin. assays.

IT 67508-63-8P

RL: PREP (Preparation)

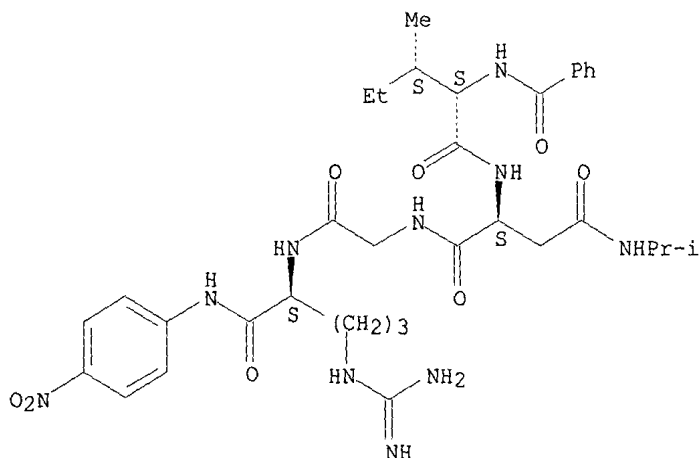
(prepn. of, as serine proteinase substrate)

RN 67508-63-8 HCAPLUS

CN L-Argininamide, N-benzoyl-L-isoleucyl-N-(1-methylethyl)-L-asparaginylglycyl-N-(4-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



● HCl

L31 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1977:107045 HCAPLUS
 DOCUMENT NUMBER: 86:107045
 TITLE: Biologically active polypeptides
 INVENTOR(S): Hamburger, Robert N.
 PATENT ASSIGNEE(S): University of California, USA
 SOURCE: Ger. Offen., 46 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|--------------|
| DE 2602443 | A1 | 19761021 | DE 1976-2602443 | 19760123 <-- |
| JP 51118702 | A2 | 19761018 | JP 1976-7400 | 19760126 <-- |
| JP 60002318 | B4 | 19850121 | | |
| AU 7612303 | A1 | 19770929 | AU 1976-12303 | 19760324 <-- |
| AU 514308 | B2 | 19810205 | | |
| GB 1539102 | A | 19790124 | GB 1976-12632 | 19760329 <-- |
| BE 840193 | A1 | 19760930 | BE 1976-165690 | 19760330 <-- |
| FR 2305989 | A1 | 19761029 | FR 1976-9232 | 19760330 <-- |
| FR 2305989 | B1 | 19791005 | | |
| CA 1087171 | A1 | 19801007 | CA 1976-249207 | 19760330 <-- |
| SE 7603897 | A | 19761005 | SE 1976-3897 | 19760401 <-- |
| SE 430058 | B | 19831017 | | |
| SE 430058 | C | 19840126 | | |
| NL 7603384 | A | 19761006 | NL 1976-3384 | 19760401 <-- |
| CH 624093 | A | 19810715 | CH 1976-4092 | 19760401 <-- |
| CA 1079721 | A2 | 19800617 | CA 1979-338393 | 19791025 <-- |
| AU 8065181 | A1 | 19810416 | AU 1980-65181 | 19801208 <-- |
| AU 531075 | B2 | 19830811 | | |
| PRIORITY APPLN. INFO.: | | | US 1975-565425 | 19750404 <-- |
| | | | DE 1976-2602443 | 19760123 <-- |
| | | | AU 1976-12303 | 19760324 <-- |
| | | | CA 1976-249207 | 19760330 <-- |
| AB | R-Asp-Pro-Arg-OH (I; R = H, H-Ser, H-Asp-Ser, H-Ala-Asp-Ser) were prepd. by solid-phase methods. Thus, Me3CO2C-Asp(OCH2Ph)-Pro-Arg(NO-2)-resin (II) was prepd. and cleaved with HBr and CF3CO2H to give H-Asp-Pro-Arg(NO2)-OH which was hydrogenated to give I (R = H). The tetra-, penta-, and hexapeptides were prepd. by extending II. I gave av. inhibitions of the allergic reaction in the Prausnitz-Kustner test of 15%, 18%, 72%, and 46% resp. H-Asp-Thr-Glu-Ala-Arg-OH and H-Arg(SO3C6H4Me-4)-NMeCH2C(OMe) gave av. allergy inhibitions of 58% and 24%, resp. | | | |
| IT | 62087-79-0P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of) | | | |
| RN | 62087-79-0 HCAPLUS | | | |
| CN | L-Arginine, N2-[1-[N-[N-L-.alpha.-aspartyl-O-(1-oxohexyl)-L-seryl]-L-.alpha.-aspartyl]-L-prolyl]- (9CI) (CA INDEX NAME) | | | |

Absolute stereochemistry.

CANELLA 09/544,644

